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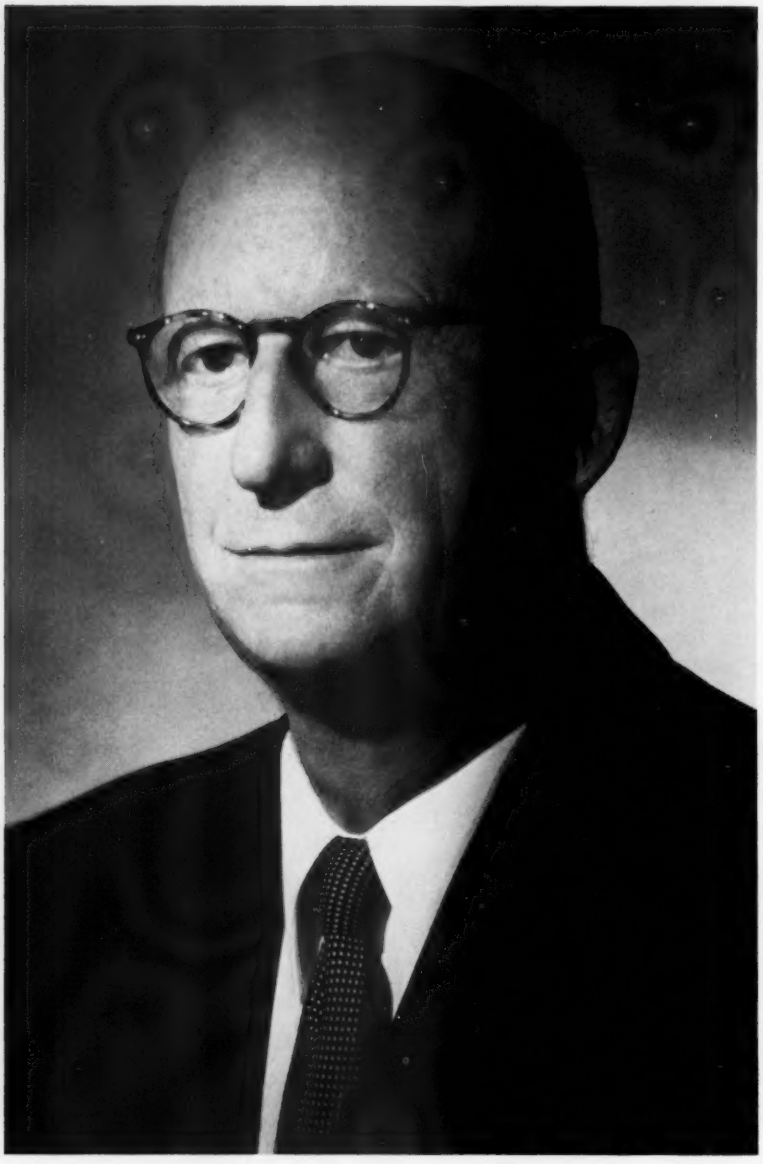

CHARLES L. MARTIN

PRESIDENT OF THE AMERICAN ROENTGEN RAY SOCIETY, 1952–1953

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THE PARTIALLY EXPLORED FIELD OF CLINICAL RADIATION THERAPY*

By CHARLES L. MARTIN, M.D.
DALLAS, TEXAS

Dr. Kerr, Dr. Barth, Members of the American Roentgen Ray Society, Ladies and Gentlemen:

IT IS with a mixed feeling of pride and humility that I accept the great honor which you have just conferred upon me. I only wish that my father might be here today to attend the opening of the first meeting of this Society to be held in our great Southwest. His was the enthusiasm of one of the outstanding radiological pioneers in this area and he would glory in the fulfillment of the many predictions which he made for the future of our branch of medical practice.

In looking back over my thirty-two years in the specialty I am tempted to wax eloquent over the many significant contributions made by you and your associates. However, I hope that you will bear with me while I make a few critical observations aimed at stimulating you to even greater achievements.

For many years radiological development in this country has shown a tendency to swing slowly but steadily into diagnostic fields and away from therapy. Curiously enough, this change has occurred during an era in which our engineers and physicists have outdone themselves in providing new devices and substances designed to generate radiant energy for therapeutic purposes. So impressive have been these contributions that the medical profession has been led to believe that the cure of cancer hinges on the development of machines operating at fantastic voltages or on some new as yet undiscovered isotope.

In many teaching institutions the radiological residents have become so involved in mathematical calculations that they seem to have lost sight of many of the clinical problems which are of major concern to the patient. The same trend can be seen in the research laboratories where the biophysicists have exhibited an overpowering urge to delve into the structure and properties of the atom rather than to study the behavior of living cells. I wish, therefore, to make a plea for a renewal of interest in our biological problems and a more intimate contact between radiological

* President's Address delivered before the Fifty-third Annual Meeting, American Roentgen Ray Society, Houston, Texas, September 23–26, 1952.

residents and patients receiving radiation therapy.

Even though radiation has been used in the treatment of malignant diseases for more than fifty years many of the basic problems remain unsolved. We sometimes lose sight of the fact that the fundamental problem in cancer therapy revolves about the delivery of a cancerocidal dose without the production of irreparable damage to the normal tissues. This principle holds good for all voltages and all radioactive materials and yet we do not know the doses needed to eradicate many malignant tumors, and exact data covering tolerance doses for normal tissues have never been properly determined for all types of therapy. Most of the available information dealing with the quantities of radiation capable of destroying the various malignant tumors has been tabulated by pathologists who confidently set down the required number of roentgens in each case without consideration of wavelength, time factor or other important variables.

It was my ambition many years ago to determine the tolerance of each normal tissue in the body but the undertaking was much too large for my modest facilities. Some large experimental laboratory should take up this essential problem. Much of the work might be done with animals if a species could be found with tissue responses similar to those observed in the human body.

The determination of adequate tumor doses would be much more difficult, particularly for the more radioresistant neoplasms. It is well known that certain tumors having an identical microscopic appearance respond differently to similar quantities of radiation. Many of us in this country believe that carcinoma growing in lymph nodes acquires a resistance not observed in the primary lesion. Certainly the blood supply in the tumor bed plays a role and perhaps other factors as yet undiscovered in the human body are of vital importance. The failure of certain radiosensitive tumors, such as those observed in the leukemias and lymphoblastomas, to remain permanently well constitutes one of our most distressing unsolved mysteries. Such problems could best be investigated on a radiological hospital service to which patients are assigned and completely cared for by a staff primarily interested in the treatment and study of sick people and the changes produced in living cells. Unfortunately, few American hospitals have such services and in many institutions patients receiving radiotherapy are under the supervision of physicians who are completely unfamiliar with the effects of radiant energy. This state of affairs is, in my opinion, usually the fault of the radiological department which is so burdened with diagnostic routines and dosage computations that the troublesome bother of patient care is sidestepped when possible.

After the establishment of tolerance doses for normal structures and effective tumor doses an intensive investigation should be started in an effort to further increase the differential between these two factors. The greatest forward step made thus far in this direction has resulted from the adoption of lower intensities and longer time factors. The economic considerations involved in the administration of treatment over very long periods of time often render such methods quite impractical and there is a great need for a careful study of the most efficient treatment periods needed for good results. The mass of time factor data collected for the lower voltages by Strandqvist and others should be rechecked and carefully evaluated. An attempt should then be made to answer many important questions. If, for instance, 4,700 roentgens given in ten days is just as destructive to cancer cells as 6,000 roentgens given in thirty days, is it imperative that the longer time factor be used to protect the normal tissues? Do the very long periods of treatment advocated by the French really produce better results than shorter periods when biologically equivalent doses are given? What is the most efficient daily dose or does the size of the daily fraction make

any real difference? Is it really true that the shorter wavelengths tend to spare the normal tissues when similar amounts of radiation are given? Do the grid techniques actually spare normal tissues or will the late effects of such intensive therapy be disastrous?

After the best combination of treatment factors has been determined some group might begin to intensify the search for a substance or physical procedure capable of protecting normal tissue against irradiation damage or of increasing the radiosensitivity of malignant cells with the hope that the more resistant tumors could then be safely treated. Perhaps some brilliant chemist will eventually produce a radioactive substance which is absorbed exclusively by neoplastic tissue. I have been guilty of adding to the rather voluminous literature dealing with irradiation sickness but I feel that most of the contributions made thus far have little practical value. Every possible avenue should be explored in an effort to discover some method of protecting the human organism against the curious toxic effects of whole body irradiation.

I am inclined to wonder whether many of the more brilliant young physicians coming out of our medical schools today are at all familiar with the intriguing and fascinating lines of investigation provided for them by therapeutic radiology. Unfortunately, the radiological residents in many of the hospitals which I have visited have adopted a pessimistic attitude towards radiation therapy based on a rather depressing experience made up almost entirely of the treatment of hopeless cancer cases often relegated to their care as a last resort following unsuccessful surgery. These men should be allowed to experience the exhilaration and sense of achievement which accompanies the complete cure of a large malignant neoplasm with irradiation alone. Such opportunities can only be provided in an institution possessing a strong radiation therapy service. Well organized tumor clinics in which surgeons and radiologists meet on an equal footing for the purpose of arriving at a fair evaluation of all available types of therapy provide the best training for residents in both fields. It has been my good fortune to work in such clinics and I have been much impressed by the willingness of my surgical confrères to cooperate with enthusiasm in the exploration of new radiological procedures which produce promising results. In fact, most good surgeons welcome the aid of an aggressive radiotherapist in their rather desperate struggle against malignant disease.

These rambling observations are presented to you with no thought of disparaging other types of cancer research. Rather it is my intention to emphasize the fact that our own field which has so much to offer has not been thoroughly explored. When you return to your various hospitals and teaching centers it is my fond hope that you will inspire some of the courageous young physicians with whom you are associated to accept the challenge of radiation therapy and elevate it to the position which it so richly deserves in this country.

3501 Gaston Ave.
Dallas, Texas

TRANSVAGINAL CONE ROENTGEN IRRADIATION IN CANCER OF THE CERVIX UTERI*

REPORT OF TWELVE YEARS' EXPERIENCE

By JOHN Y. HOWSON, M.D., BERNARD P. WIDMANN, M.D., *and* JAMES L. WEATHERWAX, M.A.

From the Radiological Clinic, Philadelphia General Hospital

PHILADELPHIA, PENNSYLVANIA

THE treatment of cancer of the cervix uteri with roentgen rays first began about 1901. In 1902 Caldwell[3] proposed administering roentgen rays to malignant lesions of the cervix through the vaginal canal. He had noted that the roentgen ray was most beneficial when the cancerous lesion was superficial and he concluded that the usual reaction in normal tissues overlying pathologic lesions could be avoided by direct contact application of roentgen radiation to the vagina. The primitive nature of the roentgen-ray apparatus at this time precluded any practical application of this idea.

In 1921 Merritt[7] revived interest in intracavitary roentgen therapy by comparing the effect of the roentgen radiation used in this manner with that of radium. The favorable comparison suggested that this method of treatment might be used when radium was not available.

Martius,[5] in 1937, championed the use of proximate roentgen irradiation on the basis that more radiation could be delivered to the parametrium than by the use of radium and percutaneous roentgen therapy.

Again, in 1938, Martius[6] points out that his aim is to increase "the radiation dosage in the entire cancerous region without exposing the surrounding healthy tissue and organs, the bladder and the rectum, to an excessive and harmful dosage." He felt he could accomplish two things by intravaginal irradiation: the delivery of an increased amount of roentgen radiation to the parametrium and the direct irradiation of the primary tumor of the cervix, causing it to disappear.

That it is possible to obtain lasting results with intravaginal roentgen irradiation was demonstrated by Teschendorf[10] in 1939. His conclusions were derived from the observation of 92 cases treated in this manner between 1929 and 1939.

Likewise in 1939 Merritt[8] again reiterated the value of pervaginal roentgen irradiation and made two additional observations: that this method of approach completely avoided any exacerbation of the accompanying infection, and that by limiting trauma of the cancer zone to the introduction of a speculum, the possibility of dissemination of cancer cells was materially lessened. He reported the use of intravaginal roentgen therapy in 112 cases with results which were superior to any previous experience.

Since Merritt's second report several contributions have been made as to the type of equipment used and the technique of applying the roentgen radiation in the vaginal canal. Erskine[4] described an expanding speculum for intravaginal roentgen therapy. In this manner he hoped to increase the field of radiation. Morrison,[9] in 1940, stated that the problem of adequately irradiating the parametrium was still unsolved. Progress, he suggested, might be made by directing the pervaginal roentgen radiation into the vaginal fornices. Wasson[11] in 1943 expanded this theory by suggesting that the treatment cones be rotated clockwise through the two lateral and the anterior and posterior fornices of the vagina.

Our favorable experience with high voltage roentgen therapy as a palliative measure through the usual external portals led us to believe that additional trans-

* Presented at the Fifty-second Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 25–28, 1951.

vaginal irradiation of these advanced lesions might enhance the degree and duration of palliation for these patients. Our interest in palliative therapy was stimulated by the high percentage of advanced lesions admitted to our clinic. In 1938 two of the present authors (B. P. W. and J. L. W.) collaborated with C. A. Behney in initiating the use of transvaginal roentgen therapy at the Philadelphia General Hospital as a possible additional palliative adjunct in the treatment of advanced cancer of the cervix uteri.

METHOD OF TREATMENT

Our experience with the treatment of 1,007 women with cancer of the cervix treated in the Radiological Clinic of the Philadelphia General Hospital since 1922 indicates that the best results are obtained in those cases receiving high voltage roentgen therapy prior to the administration of radium. This observation was made in a report from our clinic in 1944,[2] and it has become our policy to administer roentgen therapy preliminary to any other type of therapy in the treatment of this disease. At the present time and during the span of twelve years covered by this report, preliminary roentgen therapy consists of one series of 2,000 r (air) delivered through four skin portals 15 by 20 cm. with the rays directed to the tumor area, in addition to a course of 8,000 r to 12,000 r (air) administered through a vaginal cone to the cervical tumor.

The roentgen-ray factors used are as follows: Two deep therapy roentgen machines are employed in giving radiation; namely, a 200 kv. Villard pulsating unit with 0.5 mm. Cu plus 1 mm. Al filter, having a half-value layer of 0.95 mm. Cu, and 190 kv. constant potential with 0.5 mm. Cu plus 1 mm. Al filter, with a half-value layer of 1.1 mm. Cu. No attempt is made to differentiate between the two roentgen machines in treating any particular patient as the difference in half-value layers is not significant.

The depth dose for 100 r (air) for external irradiation through a 15 by 20 cm. field gives 147 r (tissue) on the skin, 102 r (tissue) at 5 cm., 56 r (tissue) at 10 cm., 30 r (tissue) at 15 cm. and 18 r (tissue) at 20 cm. The beam of radiation is angled and directed towards the center of the patient. The fields are separated front and back so as to avoid over irradiation directly underneath the skin.

The anteroposterior measurement of the patient is determined and from depth dose tables or isodose curves the total dose delivered to the center of the pelvis is obtained.

The same factors as described are used in giving intravaginal roentgen therapy. The fields vary from approximately 5 to 10 square centimeters. For every 100 r (air) the surface of the lesion receives 108 to 112 r (tissue); 5 cm. depth, 50 to 53 r (tissue); 10 cm. depth, 19–21 r (tissue); 15 cm. depth, 7 to 9 r (tissue). Eight thousand roentgens (air) delivers on an average 8,800 r (tissue) to the surface of the lesion; 4,100 r (tissue) at 5 cm. depth and 1,600 r (tissue) at 10 cm. depth. The time interval is approximately five weeks to deliver 8,000 r (air).

The majority of cases receive the external high voltage roentgen therapy first. This is given on alternate days with 150 r to each of four fields until the ultimate tumor dosage of 2,000 r (air) or approximately 3,000 r (tissue) has been reached. On completion of this external roentgen irradiation series, the intravaginal roentgen therapy is begun. The vaginal cone used for the intravaginal administration of roentgen radiation varies from 2.5 cm. to 3.6 cm. in diameter. The patient is treated three times weekly with the distal end of the vaginal cone placed directly over the cervix, with 500 r (air) being delivered through the cone at a single treatment until a total of 8,000 to 12,000 r (air) has been attained. In some instances the external roentgen irradiation and the intravaginal cone therapy have been given simultaneously. Young patients who are not debilitated by the disease and appear to be able to tolerate high doses of roentgen radiation are treated in this manner. In some instances where bleeding has been a major problem and a prominent symptom, the intravaginal course of roentgen therapy has been administered first. In our experience, this has been a more rapid means of controlling hemorrhage than external high voltage roentgen therapy.

Intravaginal roentgen therapy has also been usefully resorted to when tolerance to the external high voltage therapy is a serious consideration. Under such conditions intravaginal roentgen therapy, which is universally well tolerated, has been advantageously applied while awaiting an opportunity to continue and

complete the external irradiation. A second series of external irradiation, similar to the course described above, is given six to eight weeks after the completion of the transvaginal treatment.

In a few instances a second course of intravaginal irradiation of 8,000 r (air) has been used. In those cases where the original full course of treatment has caused complete clinical regression of the tumor, but weeks or months later a local recurrence is noted, the second course of intracavitary irradiation has been useful. It has been well tolerated with no additional risk being observed and has served to prolong further the palliative arrest of the carcinoma with a resultant longer life span.

The additional apparatus required for transvaginal high voltage roentgen therapy by a clinic equipped with a deep therapy machine and gynecologic instruments is inexpensive and easily obtained. The cone and the adapter, by which the cone is connected to the roentgen tubes, are the only unusual articles needed. Our cones are chromium-plated, brass tubes, lined with 0.5 mm. lead and varying in diameter from 2.5 to 3.6 cm. Cones should be available with either straight or beveled distal ends. An inflated rubber balloon is used as an obturator for the cone. The balloon protrudes from the distal end of the cone, and facilitates its introduction into the vagina with less discomfort to the patient. The adapter is fitted with a periscope finder by means of which the lesion can be visualized after the apparatus has been attached to the roentgen machine. A simple, flat top wooden table, 27 inches high has been used more successfully than the standard gynecologic examining table. A leaf, 18 inches long, is hinged to the foot of the table. By raising the leaf it enables the pelvis of the patient to be elevated from 6 to 12 inches, which facilitates exposure of the lesion and easier connection of the cone with the adapter. The patient's legs are comfortably supported in stirrups at the foot of the table.

The patient is placed in the lithotomy position with the buttocks on the edge of the leaf at the foot of the table. While the labia are separated with one hand, a well lubricated cone with the obturator in place is gently inserted into the vagina. The obturator is now withdrawn and the distal end of the cone placed directly over the lesion on the cervix under direct vision. We have not attempted to direct the cone to the vaginal fornices because the large number of advanced cases in our series precludes sufficient mobilization of the vaginal vault to allow this maneuver. While the cone is held in place, the roentgen-ray apparatus is moved so as to connect the proximal end of the cone with the adapter which is attached to the roentgen therapy machine.

RESULTS

Between August, 1938, and December 31, 1950, we have treated 361 cases of cancer of the cervix with intravaginal roentgen therapy as a supplement to the usual percutaneous roentgen treatment, and in some instances radon. Two hundred and twenty-five of these patients received at least two courses of high voltage roentgen irradiation through four external portals and at least one course of high voltage roentgen irradiation delivered transvaginally. This means

TABLE I

	Cases
Stage I	6
Stage II	33
Stage III	111
Stage IV	61
Stump	14
Total	225

that 136 patients of the 361 treated have been excluded from this report. Many patients selected for treatment, particularly in our early experience, were so advanced that treatment was incomplete at the time of death. Some patients failed to continue treatment and received an amount of radiation considered inadequate. A large group of patients were excluded who had received treatment elsewhere before reporting to the Radiological Clinic of the Philadelphia General Hospital.

The distribution of the 225 cases to be considered in this report into the various clinical stages is shown in Table I. It will be noted that 76.4 per cent of the cases treated in this series fall into the far advanced stages. The percentage of advanced lesions is approximately the same as the over-all incidence of advanced lesions

presenting themselves for treatment in our clinic.

Our limited small number of Stage I cases precludes any analysis of patients in this category at this time.

In 1944, Behney* and one of us (J. Y. H.[2]) reported the results of treatment of 579 patients with carcinoma of the cervix who had died on the Radiological Service at the Philadelphia General Hospital between 1931 and 1942. By observing the duration of life after admission to the service in these patients it was possible to evaluate the various forms of therapy. Using the same criteria as a basis for comparing the results of cone therapy with other forms of therapy, the patients who have died from August, 1938, to January, 1951, in this present series are compared with the results of the patients treated with roentgen radiation, and roentgen radiation and radium between 1931 and 1942.

Sixty-one patients in Stage IV have been treated with external and intravaginal high voltage irradiation. Of this number, 52 have died and their average duration of life was 13.6 months. The average duration of life of patients treated with only external high voltage roentgen therapy in the 1931–1942 series was 7.9 months.

This represents an increase of approximately 42 per cent in the duration of life of patients who had a frozen pelvis on admission to the clinic. In the 1931–1942 series, 10 patients received radon in addition to external high voltage roentgen therapy and survived an average of thirteen months. The duration of life for these 52 patients receiving external and intravaginal roentgen therapy is essentially the same as these 10 patients of the 1931–1942 series who had radon in addition to external roentgen therapy.

It is interesting to note that 9 patients in Stage IV in the present series are still living. Their average duration of life is 54.5 months as of January 1, 1951. Four of the 9 cases have lived five years. At present the five year cure rate for the 61 Stage IV cases in this series is 6.5 per cent. The five year survival rate for all forms of treatment for State IV cases in our clinic from 1923 to 1937 inclusive was 2.04 per cent.

TABLE II

STAGE IV

Series	No. of Cases	Type of Treatment	Average Duration of Life
1931–1942	161	External high voltage roentgen therapy only	7.9 months
1931–1942	10	External high voltage roentgen therapy and radium	13.0 months
1938–1950 (cone series)	52	External high voltage roentgen therapy plus intravaginal roentgen irradiation	13.6 months

Of the 111 cases in Stage III treated with transvaginal and external roentgen irradiation, 86 have died. The average duration of life of this group was 23.7 months. In the 1931–1942 series, 46 Stage III cases receiving only external high voltage roentgen therapy lived an average of 10.8 months. In the same series, 99 patients receiving external roentgen irradiation and radon died an average of 18.8 months after treatment.

The figures in Table III indicate that the average duration of life of Stage III patients treated with external high voltage roentgen therapy and transvaginal roentgen therapy is longer compared to any previous method of treatment. Intravaginal cone treatment has increased the survival rate 54.5 per cent over the average duration of life previously noted when treatment was confined to external high voltage roentgen

* Dr. Charles A. Behney, Chief Gynecologist to the Radiological Department of the Philadelphia General Hospital during the time covered by this report, has recently been succeeded by Dr. John E. Griffiths.

therapy alone. Likewise, the average duration of life in the present series shows a 20.7 per cent increase over the cases treated with roentgen irradiation and radon between 1931 and 1942.

It is to be noted that 25 Stage III cases are still living who received only external and intravaginal high voltage roentgen therapy. The average duration of life of this group is 83.5 months, or almost seven years. Of this current group, 17 cases have lived five years or longer, and in the group that died 6 cases lived more than five years. Therefore in Stage III, we have a total of 23 five year cure cases, or an incidence of 20.7 per cent. The five year survival rate previously recorded in our clinic from Stage III cases treated with roentgen radiation or roentgen radiation and radium was 13 per cent.

Thirty-three Stage II cases had supplementary treatment with intravaginal roentgen therapy. Of this number 18, or 54.5 per cent, have died. Of the 18 who died, 10 were treated only with external and intravaginal roentgen therapy. The remaining 8 patients received the same application of roentgen radiation but additionally had intrauterine radon.

The average duration of life for the roentgen irradiated group was 32.3 months, whereas the roentgen-ray plus radon group lived 39.7 months, or an average for all cases of 35.5 months. In the 1931–1942 series, 20 patients in Stage II treated with roentgen radiation and radon survived only 17.2 months.

TABLE III

STAGE III

Series	No. of Cases	Type of Treatment	Duration of Life
1931–1942	46	External high voltage roentgen therapy only	10.8 months
1931–1942	99	External high voltage roentgen therapy and radium	18.8 months
1938–1950 (cone coses)	86	External high voltage roentgen therapy and cone	23.7 months

TABLE IV

STAGE II

Series	No. of Cases	Type of Treatment	Duration of Life
1931–1942	20	External roentgen irradiation and radon	17.2 months
1938–1950 (cone)	10	External roentgen irradiation and cone	32.3 months
1938–1950 (cone)	8	External roentgen irradiation plus cone and radon	39.7 months

Our favorable impression and observation of results with supplementary intravaginal roentgen therapy in advanced stages explains the experimental withholding of radon in 10 of the 18 Stage II patients. The duration of life for this group who received only roentgen irradiation was 46.8 per cent better than the 20 patients of the 1931–1942 series receiving external roentgen therapy and radon. That radon and intravaginal roentgen therapy together enhance the duration of life is reflected in the 8 patients who survived 56.7 per cent longer than the patients who were treated only with external high voltage roentgen therapy and radon. Our results when transvaginal high voltage roentgen therapy

supplements the usual percutaneous application of roentgen radiation alone or combined with radon in advanced cases of carcinoma of the cervix has established the use of cone irradiation for all cases now entering our clinic. We conclude that roentgen radiation delivered transvaginally should be used as an additional portal for the administration of high voltage roentgen radiation in carcinoma of the cervix to supplement the conventional modes of administration of roentgen rays and radon.

EFFECTS OF TREATMENT

The close cooperation in the Radiological Department of the Philadelphia General Hospital between the radiotherapist and the gynecologist has afforded an unusual opportunity for both to observe at first hand the effects of treatment. The gynecologist has had the opportunity to examine the patient before each treatment as well as to apply the cone to the lesion and determine the exact field for irradiation. The technical factors of therapy are dictated by the radiologist.

The clinical improvement in patients receiving intravaginal roentgen therapy has been most gratifying. Local regression of the lesion with control of hemorrhage and discharge was a frequent observation. The subjective improvement with increased appetite and weight gain, a decrease in the degree of pain and an over-all increased sense of well being was an almost constant factor, except in the most extremely advanced cases that were beyond any hope of relief. Improvement, if it occurred, was apparent in most instances by the time the cone series was completed. In about one-third of the cases, subjective relief was noted midway through the course of therapy or when the patient had received approximately 4,000 r (air) to the lesion.

The systemic reaction so noticeable on the external application of roentgen radiation in cervical cancer cases was minimal. At most, a temporary moderate proctitis was noted in about one-third of the patients, but no nausea or vomiting was present attributable directly to the intravaginal administration of roentgen therapy. A mild cystitis, readily controlled and transient in type, accompanied some courses of transvaginal therapy.

In this series, there were 6 cases of intestinal obstruction. Three Stage III cases developed intestinal obstruction following the full course of irradiation. One case lived two months after therapy, at which time a colostomy was required to relieve large intestinal obstruction. A second case lived thirty-four months in all before developing intestinal obstruction, with peritonitis and death. A third case of obstruction developing in the rectum was directly attributable to postirradiation reaction six years after completion of therapy. This patient's obstruction was relieved and she is still living.

Two Stage II cases developed intestinal obstruction but in both instances radium supplemented the intravaginal and external high voltage roentgen irradiation. One case revealed a perforation of the bowel and peritonitis with no evidence of metastatic growth twenty-three months after beginning treatment, whereas the second case revealed marked widespread metastasis as a possible factor in obstruction.

The low incidence of rectovaginal and vesicovaginal fistulas in this series of cases is most encouraging. Previously it was reported by Behney[1] that the incidence of vesicovaginal fistulas in 80 patients treated in our clinic with irradiation was 18.6 per cent as noted on postmortem examination. The evidence of vesicovaginal fistulas in 86 untreated patients was 25.5 per cent at necropsy. There were 7 cases of vesicovaginal fistula, or an incidence of 3.1 per cent, in the present series of cases treated with external high voltage and intravaginal roentgen irradiation. The combined incidence of rectovaginal and vesicovaginal fistulas was 4.0 per cent, or a total of 9 cases, only 2 of which had rectovaginal fistulas. When considering sequelae of treatment and the great desire to accomplish palliative relief with the least unfavorable

side effects, this low incidence of fistulas seems to be significant. The marked difference in the incidence of fistulas between this present series and the 80 patients treated by roentgen radiation, radium, or roentgen radiation and radium combined may indicate that the use of radium, though beneficial to eradication of disease, may contribute to the incidence of fistulas.

It must be emphasized that the fistula incidence reported here is affected by the fact that this report is limited to the observation of patients who completed the full course of therapy. This would necessarily exclude many of the patients who were treated with intravaginal roentgen therapy, but who never completed the full course of irradiation but who later developed fistulas.

COMMENT

Our experience with intravaginal roentgen irradiation as a supplement to external irradiation and in some instances radium is a favorable one. The high incidence of advanced cases treated by us limits the discussion of our present results to a consideration of benefits related to palliative therapy. The increased longevity of patients treated from 1938 to 1951 is the first appreciable alteration of the previously recorded life duration in our clinic. The marked improvement in these advanced cases seems to justify the use of intravaginal therapy as an additional portal of administering roentgen therapy for palliative reasons. These results in advanced cases should stimulate an earnest attempt to evaluate the place of intravaginal roentgen therapy in the treatment of early cancer of the cervix. Our limited experience with Stage II cases that have died reveals an improved span of life for these patients treated with roentgen therapy alone over the previously reported results from treatment with roentgen therapy combined with radium, and a still better result when radium is combined with intravaginal and external roentgen irradiation. The symptomatic relief, the regression of the local lesion, the low incidence of unfavorable reactions and sequelae and the increased longevity in Stages II, III and IV of the present group of patients seem to indicate that intravaginal roentgen therapy should be a part of all radiation technique for the treatment of carcinoma of the cervix. The ease of application and the ready availability of the necessary equipment make intravaginal roentgen therapy readily available. It is our belief that the place of intravaginal roentgen therapy is not as a substitute for radium but to supplement its use and to be additional therapy for patients who formerly were limited exclusively to the benefit of external high voltage roentgen therapy. The low incidence of unfavorable sequelae is extremely gratifying, and for those interested in palliative therapy, the intravaginal application of roentgen radiation is recommended for the advanced cancer patient.

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DISCUSSION

Dr. Ralph M. Caulk, Washington, D. C. I am most happy to be invited to discuss this paper. I was associated with the late E. A. Merritt when he revived this technique in October, 1936. As of January 1, 1951, we have used this approach in the definitive treatment of 556 cases of cervical cancer. As a matter of fact, our entire treatment technique, that is, external roentgen therapy, intracervical and intrauterine radium is designed to complement the transvaginal approach.

I wish to cite the following figures to prove to you that the technique as employed by us has great potentialities. Prior to 1945 we treated 40 cases of Stage 1, revised League of Nations classification, cases of cervical cancer by the transvaginal approach *only*. These patients had no radium nor external roentgen therapy. Sixty-three per cent of these cases have survived from five to fourteen years. Our cure rate in all of our material in this stage is the same—61 per cent, regardless of whether we added radium or external roentgen therapy, or in any combination. Martin of Dallas reports a 61 per cent cure rate by his technique with identical clinical staging of his material. Lampe at the University of Michigan reports a 61 per cent cure rate with their techniques in identically staged material.

In order to accomplish this, however, the transvaginal technique must be exploited to its fullest advantage. Therein lies my greatest criticism of the work of the present authors. They use a metal cylinder with a maximum field covered at the level of the cervix of 3.5 cm. in diameter, thus limiting the area covered and the depth dose, whereas with the translucent specula that we employ, an area up to 6 cm. in diameter may be covered at the level of the cervix.

The authors use a periscope, which is not necessary. If one will use the largest and the longest speculum that the vagina can accommodate, the vagina becomes completely filled with the speculum, and therefore it cannot move and the lesion must remain exposed at the open end. The periscope also increases the anode-cervix distance, consequently rendering the treatment time considerably longer. The authors take five and a half weeks to give a dose that we routinely give in nine to ten days. It is not stated in the manuscript how long the authors require to give their total course of external roentgen therapy. I hope Dr. Howson will tell us how many days are required to treat a patient in their clinics.

You can see why I believe that the authors have not exploited the technique to its fullest advantage. At no place in my copy of the manuscript did the authors state what clinical classification was used. As you know, there is a College of Surgeons classification, there is a Schmitz classification, there is the old League of Nations classification and the revised League of Nations classification. These are all different and it must be stated which classification is used if one is to evaluate end results by clinical stages.

The statistical data are difficult to evaluate. One hundred and thirty-six cases were excluded from the report, indicating selection, but not stating why. It is obvious, however, that the authors were dealing with advanced cancer in almost all of their cases. They have shown without doubt that the transvaginal technique is a very effective approach, prolonging the lives of these patients with results comparable to any other method.

Dr. J. A. del Regato, Colorado Springs, Colorado. It is altogether appropriate that our meeting in Washington should include a discussion of transvaginal roentgen therapy, as a posthumous tribute to the kind gentleman and genial radiologist, Dr. E. A. Merritt, who was responsible for the serious study of this approach to the treatment of carcinoma of the cervix.

I do not wish to repeat criticism that has already been made nor to distract from our comment by remarks on lesser aspects of this problem. We feel it is only important to emphasize that the merit of transvaginal roentgen therapy consists in permitting the utilization of the external pelvic irradiation to greater advantage than when it is combined with radium therapy. The use of transvaginal roentgen therapy eliminates overdosage at the midline which, when radium is used, prohibits further irradiation and limits the usefulness of the external treatment. In our opinion, no one is

justified in replacing radium therapy by transvaginal roentgen therapy who has not revised his plan of external treatment to permit more homogeneous irradiation of the entire pelvis and lateral extension of the area of effective dosage.

DR. ROBERT R. NEWELL, San Francisco, California. I have long been of the opinion that radium could cure the local lesion in the cervix. I have long been impressed by the statistics from all over the world which show a remarkable parallelism between the failures in any group and the percentage of lymphatic metastases for that group, as though one were pretty uniformly curing the primary lesion and failing only because of the metastases. Under those circumstances, an improvement by a different attack on the cervix itself would not promise anything.

I still cannot see how transvaginal therapy can do a better job on the cervix than radium can. All I can see now is that if statistics such as we have just listened to are confirmed—and the statistics are impressive—it must be because the operation of placement of the radium in the cervix itself increases the incidence of metastases, something which we had taken for improbable in the past but which perhaps ought to be reconsidered.

DR. HOWSON (closing). I wish to thank the discussors, Dr. Caulk, Dr. del Regato and Dr. Newell, for their comments. In answer to Dr. Caulk's question as to the length of time that we take to treat with the external series, it takes approximately three weeks.

We use the Schmitz classification in determining the stage of the cancer. We do not consider these patients to be a selected group for our presentation. We have been trying to evaluate the effects of intravaginal roentgen therapy and to include many semi-treated patients in our statistics would not allow us to evaluate the true results of our treatment plan.

We are also aware of our limitations as to the field which we used for irradiation. As noted in reports from some clinics, they frequently will alter their technique from year to year so that at the end of a ten year span the number of cases for any given technique is too small for real evaluation. We have kept our technique at the original level for ten years in order to try to arrive at a fair and proper evaluation of this pattern of therapy.

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CANCER OF THE ESOPHAGUS*

SURGICAL CONSIDERATIONS

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OF ALL the patients admitted to Memorial Cancer Center, approximately 3 per cent are found to have a malignant neoplasm located somewhere in the gullet. This ratio of cases and the incidence of the disease in general, at least in Metropolitan New York, has remained constant during the past twenty-five years. The number of admissions on our service varies year to year from 36 to 59, and the total series available for study consists of 1,434 cases.

Knowledge of the etiological factors involved in the development of cancer of the esophagus is no more definite today than it was in 1933, when I first reported on 506 cases of this disease.[6] At that time oral sepsis, dental defects, badly kept teeth, and ill fitting dentures leading to poor mastication and resulting in esophageal trauma, esophagitis, and chronic ulceration were thought to be the most important predisposing factors in the etiology of esophageal cancer.

The histopathology of esophageal cancer plays an important role in our thoughts regarding the surgical approach to this disease. Relatively few highly anaplastic and undifferentiated epidermoid cancers occur in the esophagus, and on this basis alone the disease should be theoretically well suited to surgical management. Eighty-eight per cent of the lesions are squamous cell cancer and the others are, for the most part, adenocarcinoma. These adenocancers have their origin from mucous glands or ectopic gastric mucosa and they occur at any level in the esophagus. Primary sarcoma of the esophagus is rare and only 4 cases are included in this series (0.28 per cent), but 1 of these patients is a five year surgical cure, indicating possibly a fair prognosis for this uncommon disease.

Although predominantly a disease of males, the ratio of 6 males to 1 female, a high percentage of females come to surgery and more of them present resectable cancers than is the case with the males. Of seventy-six esophagectomies, 53 were males and 23 females.

The age distribution follows much the same pattern as for other malignant diseases in that the majority of patients are between forty-five and sixty-five years of age. Of surgical significance, however, is the rather large group of patients who are between the ages of sixty-five and eighty. At one time, the consensus was that patients in this advanced age group were unsuitable for radical esophageal cancer surgery. It was thought that concomitant geriatric problems, a limited life expectancy, and the magnitude of the surgical undertaking all contraindicated radical surgery. It has been gratifying to find that our apprehension on this score has been exaggerated, as we have successfully carried out esophagectomy on a consecutive series of 25 patients between the ages of sixty-five and eighty with only 1 operative death, a patient aged sixty-seven, and among the 10 patients between the ages of seventy and eighty who had esophagectomy there was no postoperative mortality.

Surgical measures for the management of cancer of the esophagus may be placed in two main categories. In the first are those procedures which are directed toward providing the patient with a measure of relief of his symptoms and a degree of palliation or growth restraint. Endoscopic dilatation, exploratory thoractomy with implantation of gold-filtered radon seeds, gastrostomy, esophageal gastroesophageal by-pass (which is comparable to palliative gastroenterostomy), and many other types

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of operation have been employed in advanced, nonresectable cases in an attempt to provide adequate nutrition and prevent starvation. In the second category are those major surgical undertakings which have for their aim removal of the cancer and re-establishment of the esophageal gastric continuity.

The most common and probably the most satisfactory of the palliative surgical procedures for advanced esophageal cancer is the Janeway gastrostomy. In these poor risk patients, the operative mortality is 5.8 per cent.[2,7] Prior to the adoption of the Janeway type of gastrostomy, the operative mortality had been 18 per cent in a series of 172 consecutive cases. Since 1928, gastrostomy by the Janeway technique has been performed at Memorial Hospital in 441 instances. Some of these operations were initial steps for the Torek type of esophagectomy, others were preliminary steps in the technique of applying intracavitary radium radiation. Many were done in order to provide adequate patient nourishment during a prolonged course of supervoltage roentgen therapy, but the majority were merely palliative gestures. In looking over our yearly record of operations, it is apparent that radical esophageal surgery has steadily become more feasible and safer and, as a consequence, fewer gastrostomies are now being performed. For example, in 1939, which was before our first esophagectomy, we had 22 gastrostomies for cancer of the esophagus, and by contrast, in 1950 there were only 8 gastrostomies and 13 surgical esophagectomies.

In the second and more hopeful group, are those surgical operations which are aimed at curing the patient with esophageal cancer. Such procedures require esophageal resection in part or in toto, and in this study are included 76 such esophagectomies of which 72 have been carried out in the past five years.

PREOPERATIVE CARE

A major step in the preoperative management of these patients is esophagoscopy and bronchoscopy. These endoscopic procedures should be performed by the surgeon in charge of the patient. In order that the operator may determine for himself such details as the condition of the vocal cords, the level of the growth, its mobility, and whether or not there is evidence of mediastinal, bronchial, or tracheal invasion.

Surgical operability having been determined, the patient is then critically studied by a specially trained internist who evaluates him from the general medical viewpoint, and restores his electrolyte balance, improves the cardiovascular status, restores the blood factors and corrects, as far as possible, the inanition and dehydration so commonly present. The internist charged with this responsibility finds very few patients who cannot be operated upon because of age, debility, or heart disease, but many are denied surgery because of extension of the cancer into the cervical lymph nodes, the mediastinum, the trachea, bronchus, or other contiguous structures. Again we are faced with the problem of late diagnosis.

The next important step in preparation for surgery is a consultation with the chief of anesthesiology. This meeting permits preoperative study of the particular patient and his individual requirements, and allows for unhurried decisions as to preoperative medications as well as to what anesthetic agents are best suited to the case in point. Here again, an adverse decision by the consultant may result in cancellation of the proposed operation, but this is seldom the case.

ANESTHESIA

The success of esophageal surgery is in a large measure dependent upon a coordinated team effort, and the anesthetist is a key member of this group. For cancer of the cervical esophagus which we now approach through the neck and upper sternum, the anesthesia most commonly used is a combination of d-tubocurarine and pentothal sodium and oxygen administered through an intratracheal tube or a tracheos-

tomy. As in all radical head and neck procedures, an abundant supply of oxygen is administered at all times and the blood volume is maintained by continuous, adequate transfusion replacement.

When a transthoracic approach to an esophageal cancer is undertaken, the anesthesia problem is then complicated by the alterations in the cardiopulmonary physiology brought about by opening the chest, collapsing one lung, and allowing the mediastinum to shift and remain shifted for long periods of time. For the most part, ether and oxygen are dependable anesthetic agents, but I personally prefer cyclopropane. The conbination of curare, sodium pentothal and oxygen has been used only in a few cases and is not recommended.

SURGICAL ESOPHAGECTOMY

Of the greatest importance are those operations conceived with a view to completely excising a cancer of the gullet and re-establishing the continuity of the alimentary canal. Such procedures may be divided into three main varieties depending on the level of the growth. Perhaps it is not by chance alone that cancer of the gullet most frequently occurs at the three areas of anatomical narrowing; namely, the first or cervical portion; second, the upper one-third of the thoracic esophagus where the aorta and left main bronchus are in contact with it, and third, the lower or cardiac portion of the esophagus where the diaphragmatic hiatus accounts for a moderate narrowing.

Technically satisfactory operations have been evolved for cancer at these three different levels, but only in the case of the cervical lesions is one able to do a fairly adequate cancer operation and remove not only a safe portion of the gullet above and below the lesion, but also the lymph node drainage bed in continuity with it.

CANCER OF THE CERVICAL ESOPHAGUS

Successful surgery for cancer of the cervical esophagus dates back to Czerny[1] in 1877, but Mikulicz[3] in 1884 was the first to successfully excise the cervical esophagus for cancer and reconstruct it with a plastic flap. The first cured case of this type, however, was one treated by Sir Wilfred Trotter in 1927 and reported by him in 1937.[5] My first case was operated upon in June, 1940, and the patient is now alive and well eleven years later.[8] In this case a rectangular trap-door incision was made and the sternomastoid muscle, strap and omohyoid muscles and underlying lobe of thyroid gland were removed to obtain exposure and mobilize the esophagus and the cancer. The skin flap was then placed under and behind the esophagus, and at a later date the esophagus with its cancer was excised. A skin-lined cervical esophagus was fashioned by plastic procedures at a later date. This initial case was successful, but several subsequent cases operated upon by this technique were failures. There were three reasons for failure: first, metastasis to cervical and upper mediastinal lymph nodes; second, recurrence at the upper or lower margins of esophageal resection; and third, invasion of disease into the trachea or larynx.

Our present operation for cancer of the cervical esophagus was evolved over a period of years in an effort to prevent the above causes of failure. It consists of the following steps: First, a complete radical neck dissection is carried out on the side of the greatest tumor prominence, or on the side where metastatic lymphadenopathy is suspected. The sternal manubrium is then removed and the hyoid bone shelled from its bed. The strap muscles are transected inferiorly and the contralateral sternomastoid muscle transected above and below, and, although the internal jugular vein on the contralateral side is usually preserved, one may still do a fairly adequate but limited lymph node dissection on this side. The trachea and the esophagus are then cut across at the lowest convenient level and the neck mass, which then includes the tissues of both the right and left neck dissections, the complete thyroid gland, the cervical esophagus, the larynx, and the first portion of the trachea, is then

separated from the carotid arteries, the vagus nerves, and prevertebral fascia. The superior transection is then made through the bed of the hyoid at the level of the base of the tongue and inferior tonsillar pillars. The trachea is attached to the sternal defect and the skin flaps are sutured to the pharyngostome and to the esophagostome.

There have been no operative deaths in the small series of cases so treated (14 cases resected—8 radical resections), and strangely enough no case of tetany has developed even though all thyroid and parathyroid tissues were apparently sacrificed. Restoration of function is obtained by plastic surgical procedures, employing either lateral skin flaps or a migrated tube pedicle graft. One patient has gained 60 pounds in weight, and another more recent case has gained 25 pounds and now has a usable esophageal voice.

In an assignment limited to a discussion of surgical management, it is not possible to discuss other methods of treatment, but in order to maintain balance, it is well to remember that treatment by irradiation has much to offer in cancer of the esophagus, and I have reported 2 cases of cervical esophageal cancer treated by irradiation which have survived more than ten years.

CANCER OF THE THORACIC ESOPHAGUS

The first successful excision of the thoracic esophagus for cancer was by Franz Torek[4] in 1913, and yet twenty-five years later (1938) when the first attempts to duplicate his procedure were made at Memorial Hospital, the operative mortality was still in the neighborhood of 60 per cent. The Torek operation had the advantage of removing the entire esophagus and thus eliminating the possibility of local recurrence due to microscopic, submucosal spread of disease upward or downward by way of the mural lymphatics. Its great disadvantages were the draining esophageal fistula above and the gastrostomy fistula below. Attempts to bridge the gap between these two and permit the patient to assimilate his own saliva and take nourishment by mouth were seldom satisfactory, although many ingenious devices and methods were employed.

When the cancer is located between the level of the aortic arch and the superior thoracic aperture, we employ an operative procedure which is known as the right-sided, combined, thoraco-abdominal operation. A posterolateral incision is used and the chest entered through the bed of the resected right sixth rib. The azygos vein is transected and the mediastinal pleura incised from apex of chest to diaphragm and the esophagus mobilized. The incision is then extended and the abdomen opened and the stomach mobilized, maintaining its blood supply by preserving the vascular arch formed by the anastomosis of the right and left gastro-epiploic arteries. The diaphragmatic hiatus is manually dilated and the stomach passed upward through it into the chest. A pyloroplasty may be done before the abdomen is closed.

If the selected proximal line of esophageal transection is so high in the apex of the chest as to make the gastroesophageal anastomosis technically difficult, or if there is any question of disease extending upward into the cervical esophagus, it is best to make a cervical incision and bring the stomach out through this neck opening where the anastomosis can be readily carried out under direct vision. Two such cases have recently been successfully done in this fashion.

CANCER OF THE LOWER THIRD OF ESOPHAGUS

Malignant disease located in the abdominal esophagus, or between the diaphragm and the level of the inferior pulmonary vein, has been successfully managed, from the technical standpoint at least, for some years. The approach is through the left lower chest and diaphragm. This will usually provide adequate exposure for wide resection and gastroesophageal anastomosis. From the cancer standpoint,

these lesions having their origin in the lower third tend to spread early by way of the lymphatics to the perigastric and periaortic lymph nodes, and metastasis to the liver usually occurs at an early stage. The same hazards obtain, and the same likelihood of recurrence or metastasis must be accepted, as for gastric cancer. The operative measures are technically satisfactory, but from the cancer viewpoint, they leave much to be desired, and perhaps no adequate cancer operation is possible for disease in this region, and only the very early cases will be salvaged.

OPERATIVE MORTALITY

One would expect a high mortality with the Torek type of esophagectomy which was in vogue prior to the advent of chemotherapy, antibiotics, and modern anesthesia. In this series there were 7 Torek operations and 2 postoperative deaths, or 28 per cent.

Of the 33 esophagectomies plus esophagogastrostomy performed through a left thoracodiaphragmatic approach, there were 3 postoperative deaths, or 9 per cent. Of the 17 right, combined, thoraco-abdominal esophagectomies, there were 3 postoperative deaths, or 23 per cent.

A total of 14 cervical esophagectomies were performed and 8 of these were of the radical type and all required several subsequent operations for plastic reconstruction (1 patient had 7 such procedures), and yet there was no operative mortality. In all, 71 esophagectomies were done and there were 8 deaths, or 11 per cent.

CONCLUSIONS

In reviewing the course of surgical events during the past twenty-five years relative to cancer of the esophagus, it is apparent that much has been accomplished. The operative mortality has been brought within reason, more patients are seeking help at a resectable stage of their disease, and the range of resectability has been extended. Serious surgical resections are now possible in the older and more debilitated age group. And, finally, palliative resection and gastroesophageal anastomosis with reestablishment of normal alimentation is a boon to the patient with incurable esophageal cancer.

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CARCINOMA OF THE EYELIDS*

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CARCINOMA of the eyelids is a dangerous disease because of its proximity to important structures. It may cause severe changes in the function of the eyelid and underlying tissues, and loss of vision in the involved eye and even loss of life may result. The choice of the method of eradicating the lesion must be seriously considered since it is important to preserve the function of the eye and its adnexa while removing the lesion completely. In this paper, an analysis of four methods of irradiation of lesions of the eyelids will be presented.

DEFINITION

The eyelids extend to the upper and lower orbital margins and include the medial and lateral canthi. Since "canthus" refers only to the angle at the junction of the upper and lower lids, we are considering lesions arising within 3 mm. of this point as canthal lesions. In addition to the lesions that arise on the eyelids proper, we are including in this study those which arise between the bridge of the nose and the medial canthus and those at the junction of the eyelids with the cheek, temple, or eyebrow.

INCIDENCE

Various studies indicate that the eyelids are involved in from 2.73 to 55 per cent of cutaneous cancers.[7,13,14,23] Clinical and histopathologic study of all types of tumors involving the eyelids revealed 15 per cent to be malignant.[5,20,30]

TABLE I

AVERAGE AGE

All patients	62.9 years
Basal cell	60.2 years
Squamous cell	61.5 years
Intermediate cell	67.1 years

The average age of patients with basal cell carcinoma seen at the State University of Iowa Hospitals was 60.2 years; the average age of patients with squamous cell carcinoma was 61.5 years, while the average age of patients with intermediate cell carcinoma was the highest with a 67 year average (Table 1). Seventy-eight per cent of our patients with epithelioma of the lids were over fifty years old. Compared with population age statistics it is seen that the older the individual, the more susceptible he is to the development of cancer in this region.[13]

The majority of epitheliomas occur in males, the incidence ranging from 52 to 76 per cent in most series.[3,13,14,24,27,33] In a series of 109 private patients reported by Robinson,[32] 52 were males and 57 females. Dollfus[12] reports that 57 per cent of his patients with carcinoma of the eyelid occurred in females. In our series of 131 patients, 94 (71.7 per cent) were males.

It is generally believed that squamous cell epitheliomas occur most frequently at the junction of two different types of epithelium.[33] This condition exists in two areas: (1) at the junction of the conjunctiva and the skin of the eyelid, and (2) at the junction of the conjunctiva and the cornea.[3] The former is by far the more frequent site of involvement. H. E. Martin,[27] however, believes that the majority of the lesions begin on the skin of the eyelids near to, but definitely separate from, the palpebral margin. Other lesions arise from the skin apparently farther away from the palpebral margin and do not involve this structure until they become moderately or far advanced.

Epitheliomas of the eyelids are histopathologically divided into three groups in the order of their frequency: (1) basal

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cell (44–86 per cent); (2) squamous cell (7–25 per cent); and (3) basosquamous or intermediate cell carcinoma (0–37 per cent).[2,3,13,23,30,33] In our series of 133 patients, 86 patients with 87 lesions were proved histopathologically. Sixty-three (72.4 per cent) lesions were basal cell, 13 (15.0 per cent) were squamous cell and 11 (12.6 per cent) lesions were intermediate cell (Table II).

Anatomically, epitheliomas occur more commonly on the lower lid and about the medial canthus. We have attempted to classify our series anatomically into those of the upper and lower lids and medial and lateral canthus in a similar manner. Considerable difficulty was encountered in classifying the location of some of the lesions, however. Many involved two and occasionally three regions. Large lesions were assumed to have arisen at the site of their greatest bulk although any clues in the history indicating point of origin of the epithelioma were considered. Of 133 lesions, 73 (54.9 per cent) involved the lower lid, 15 (11.3 per cent) the upper lid, 34 (25.6 per cent) the medial canthus and 11 (8.2 per cent) the lateral canthus (Table III). In this study, 80 per cent of the lesions occurred on the lower lid and inner canthus. Of the 87 lesions which were proved histopathologically, the grouping was found to be essentially similar to the grouping of all lesions. The relation of site and cell type of the lesions is shown in Table IV.

Table II

HISTOPATHOLOGIC VERIFICATION

Type of Lesion	Number	Per Cent
Basal cell	63	72.4
Squamous cell	13	15.0
Intermediate cell	11	12.6
Total	87	100.0

Table III

LOCATION OF LESIONS

	Number	Per Cent
Lower lid	73	54.9
Upper lid	15	11.3
Medial canthus	34	25.6
Lateral canthus	11	8.2
Total	133	100.0

ETIOLOGY

Several etiologic factors may be suggested for the development of carcinoma of the eyelids. Benedict and Asbury[1] favor a congenital origin, in that the epitheliomas arise from the epiblast. They may therefore start in surface or glandular epithelium or "they may be congenitally sequestered epidermal masses, moles or nevi."

Another factor is long exposure to a chronic irritation such as coal tar products, sunlight, and roentgen rays.[18,27,33] Chronic irritation or trauma as an etiologic factor is given as 17.6 to 56 per cent.[3,13,15,36] However, in a series of 1,000 cases of malignant neoplasms about the eye, Lane[24] found that about three-fourths of the patients had sedentary occupations or lived and worked

Table IV

LOCATION OF HISTOPATHOLOGICALLY PROVED LESIONS

Location	Number		Basal Cell		Squamous Cell		Intermediate Cell	
Lower lid	46	52.8%	34	73.9%	3	6.5%	9	19.5%
Upper lid	12	13.7%	7	58.3%	4	33.3%	1	8.3%
Medial canthus	22	25.3%	18	81.8%	3	13.6%	1	4.5%
Lateral canthus	7	8.0%	4	57.1%	3	42.9%	0	0.0%
Total	87	99.8%	63	72.4%	13	15.0%	11	12.6%

indoors without much exposure to sunlight or other carcinogenic agents.

Senile changes in the skin which occur in the aged are also contributing factors in developing neoplasm.[18] Driver and Cole,[13] in their large series of cases, found that in 47.2 per cent of their patients senile or seborrheic keratoses preceded the malignant lesions or were present on the face concurrently with a malignant lesion found elsewhere on the face or neck, and not uncommonly they present a different histopathologic structure than those of the eyelids. Although accurate data are not available, we were impressed by the number of precancerous and malignant lesions of the face associated with the carcinoma involving the eyelid.

CLINICAL ASPECTS AND SYMPTOMS

The most common clinical types of epitheliomas of the eyelid are the cystic, nodular, ulcerating, invading and fungating lesions.[19] They may be single or multiple. The lesion may begin either as a small nonulcerating nodule with or without a central depression or it may begin secondary to a keratosis which usually ulcerates early. As the nodule slowly enlarges, a pearly translucency appears with a faint telangiectasis over the surface. Ulceration usually occurs when the nodule has reached a diameter of 5 to 6 mm., although a basal cell lesion may increase to 1 cm. or more with intact overlying epithelium. When the central area breaks down it presents a depressed, ulcerating, granulating surface covered with crusts. When the lesion arises on the palpebral margin, ulceration is commonly present from the beginning.

There are few subjective symptoms until the lesion has reached 8 or 10 mm. in size or has involved the palpebral margin, conjunctiva or medial canthus. The patient may then complain of a scratching or burning sensation, reddening of the eye or increased lacrimation, the latter due to stenosis of the canaliculi.[33] Pain or discomfort, however, may be severe but are absent until there is considerable ulceration or infection[27] or involvement of the medial canthus.[33] Because of the mild symptoms and the usually slow-growing nature of the tumor, patients frequently delay seeking medical aid. Only 20 per cent of 464 cases in Birge's series[2] sought aid during the first year. In a series of 493 cases of carcinoma of the eye, Lane[24] found that the interval following onset of symptoms until the patient saw a physician averaged 4.5 years. The lesion may be present from two months to twenty years or more before treatment is instituted.

Both the basal cell and squamous cell carcinomas are locally malignant, invading and destroying adjacent tissues, and the lesion may pursue one of several courses. It may grow outward from the eyelid producing a bulky, fungating tumor or it may erode the entire free margin of the eyelid without reaching any great bulk and without invading the orbit.[27] The orbit may, however, become involved without extensive damage to the lid. There is no evidence that the globe itself is invaded by direct extension of the growth except possibly in the late stages of an untreated or inadequately treated lesion.

Untreated basal cell carcinomas run a chronic course, as much as thirty to thirty-five years elapsing until the patient succumbs to complications resulting from deep invasion or other causes. Squamous cell carcinomas tend to run a shorter course with death commonly occurring from metastases to the corresponding preauricular nodes and later to the cervical nodes.[27]

DIFFERENTIAL DIAGNOSIS

A lesion such as a papilloma, nevus, fibroma, granuloma molluscum contagiosum, sweat gland adenoma, malignant melanoma and others, if atypical, may be difficult to differentiate from early epithelioma.[19,30] Histopathologic study is always advisable and frequently necessary for a correct diagnosis.[5,27,35] A suspected melanoma, however, should never be biopsied but should be excised widely. Its response to irradiation is poor.

TREATMENT

In general, the choice of treatment depends upon the ability of the surgeon or radiologist, the methods available to him and the nature of the lesion to be treated. In small lesions up to 5 mm. in size, Hasley[20] believes irradiation is the treatment of choice. However, if a biopsy of the lesion is necessary, simple excision is probably preferable.[2] Benedict and Asbury[1] believe the use of excision followed by radium application, surgical diathermy or fulguration the best form of treatment. Robinson[32] believes that electrodesiccation followed by radium application is the treatment of choice in early cases. Birge[3] used surgery alone or in combination with irradiation on 53 cases of squamous cell carcinoma. If, however, the lesion involves the medial canthus, the treatment of choice is irradiation because of the impossibility of restoring the lacrimal canaliculi by a plastic procedure when this structure is removed. Larger lesions, over 6 mm. in diameter, or lesions involving the palpebral surface are better treated by irradiation than by surgery.[20,27] The advantage is primarily in the better functional and cosmetic results. Far advanced lesions with extension into the orbit require radical surgical removal or a combination of irradiation and excision. If the lesion extends into bone, radical surgery is the treatment of choice, and even this may not be effective.

IRRADIATION WITH RADIUM AND RADON

Since the discovery and the increasing knowledge of the properties and better control of roentgen rays and radium, irradiation has become increasingly more effective in the treatment of carcinoma of the eyelids.

The technique in the use of radium varies with the therapist. Various sizes, shapes and strengths of radium plaques in single and multiple application are used. Some authors[9,10,12,19,23,33] prefer radium therapy alone; others[1,13,32] use it extensively in combination with various forms of operative procedures in all sizes and types of lesions. Interstitial radium, or radon alone or in combination with plaques, has been used extensively in some clinics.[9,10,12,19,23,32,33] A recent article by Charteris[10] outlines a rapid radium implantation method for basal cell carcinoma giving a total dose of 3,000 gamma roentgens in thirty hours.

Radon is being used frequently both interstitially and in plaques.[9,26,27,32,37]

The use of radium or radon under competent control gives a high rate of cure. It causes minimal scarring and gives good cosmetic results. Muscle control is usually retained. However, damage to surrounding normal tissue must be considered and protective measures taken. Protection of the orbital structures is difficult. When using interstitial radium or radon in the lid and a lead shield of 2 mm. thickness behind the lids, 25 per cent of the emitted gamma rays strike the cornea and 6 per cent reach the lens.[33] When a surface plaque is applied, using 3 mm. brass and 1 cm. distance in addition, 60 per cent[26,37] of the beam reaches the conjunctiva and up to 30 per cent reaches the lens.[26] Watson and Wuester[37] and H. E. Martin[26] find that, following implantation of gold radon seeds, the conjunctiva and lens receive 40 per cent and 10 per cent of the gamma rays respectively. The changes in normal structures following irradiation may be a serious complication and will be considered later.

ROENTGEN IRRADIATION

The disadvantages of radium stimulated attempts to find a roentgen tube which would combine the advantages of radium with the economy, efficiency and convenience of roentgen rays. Attempts to use deep roentgen therapy proved unsatisfactory because of inability to handle the machines skillfully and the technical difficulty in securing the desired effect to a small delimited volume of tissue. The resultant damage to surrounding tissues sometimes was nearly as serious as the disease.

With the advent of more flexible roentgen machines using 100 to 133 kv. and shorter (10–30 cm.) target skin distance, improvement in the technique with resultant cures and fewer secondary reactions was obtained. A single massive or "hyperintensive" dose (1,000 to 10,000 roentgens) has been given usually alone or occasionally in combination with interstitial irradiation. A large total dose may be fractionated.[27,34] Not over 15 per cent of the beam of radiation passes through a 1 mm. lead shield. Although fewer complications result following use of this method of therapy, an undesirable effect remaining is the radionecrosis of bone or cartilage which may be in close proximity to the irradiated lesion.

Because of the expense in buying and using radium, Chaoul succeeded in combining the advantages of radium therapy with the advantages of roentgen therapy in a new tube. This uses a short distance with low voltage in the production of soft, low penetrating rays.[4,17] Lesions lying in close proximity to bone or cartilage can be successfully treated with not more than a minimal undesirable effect, because of the "limitation of depth effect by producing a steep energy gradient."[26] The latter is obtained by decreasing the target skin distance and primary voltage delivered to the tube. An advantage of this method of therapy over radium therapy is the convenience to the patient. It is particularly helpful in the aged, infirm and psychiatric individuals who cannot tolerate long treatments.[21,22] In common with radium treatments, the voluntary muscle control and the canaliculi are uninjured. Pendergrass, Hodes and Garrahan[31] listed Ernst, Frick and Ott, Chaoul, Morison, Hugo and Mayneord as having published monographs on the physics of short distance, low voltage therapy. Braestrup and Blatz[4] have also contributed to the literature on the physics of short distance, low voltage therapy.

Single massive doses have been given varying from 2,500 to 4,000 roentgens, using the Chaoul tube. Most treatments are carried out, however, by divided doses varying from as low as 100 r to 800 r to one field daily. The average dose is 500 r daily, with the total dose averaging between 4,500 and 6,000 r given in ten to twelve days. As much as 9,000 r has been given in twenty-five days without ill effects.[16,17,31] As much as 10,000 to 20,000 r as a cauterizing dose has been given at one sitting to a superficial lesion using the Phillips tube.[21,22]

CAUSES OF FAILURE IN IRRADIATION

The principal causes of failure are (1) inadequate coverage of the lesion; it is necessary to include about 5 mm. of normal appearing skin about the lesion; (2) inadequate dosage; and (3) "radioresistance" of the tumor may be additional factors in the failure to sterilize the tumor; (4) extent of the lesion with involvement of bone, tarsal cartilage and conjunctiva.[13]

PROTECTIVE MEASURES

Because of irradiation reaction and complications, it is desirable to protect all tissue which does not contain carcinoma. Various sized plaques of radioactive element are used with or without lead shields to protect adjacent skin. Interstitial radium or radon is placed in such a manner that the major portion of its effect is localized to the tumor. When roentgen therapy, particularly short distance, low voltage therapy, became more popular, lesions could be easily outlined by cones, or "lead cutouts."

Shields of various heavy metals are also inserted beneath the eyelids to protect the deeper structures. Formerly we used lead shields but now use gold shields almost exclusively. The gold shields, 1 mm. thick, have been made in two sizes and are easily slipped beneath the eyelids following complete anesthesia and lubrication of the globe. They give complete protection when the short distance, low voltage therapy tube or intermediate therapy tube is used.

COMPLICATIONS FOLLOWING IRRADIATION

The complications which occur in the lids and conjunctiva include ectropion and entropion due to scarring. The deformity,

if severe, may necessitate surgical correction. There may be obliteration of the fornices with restricted movement of the globe, stenosis of the canaliculi and lacrimal duct with resulting constant lacrimation and dacryocystitis. Atrophy of the lacrimal gland resulting in a painful dryness of the globe rarely occurs. More rarely an "erysipeloid" reaction may be seen.[11]

The cornea may show ulceration as a result of an excessive dose of radiation or it may be incident to the insertion or removal of a shield.[11]

Radionecrosis may occur as a delayed reaction about three months after intensive irradiation. Diminution of sensation is the earliest sign. Pain is not an outstanding feature. A deep ulcer may require months to heal or it may progress to perforation of the eyeball.[11,28] Tarsorrhaphy is frequently done to prevent formation of opacities. A dreaded complication of radiation therapy of ocular lesions is a cataract.[3] Although it is observed as a late complication it may appear soon after treatment, especially in children. P. Martin [29] describes a case in which a cataract appeared three days following completion of treatment and became mature in seven weeks. In older patients, radiotherapy may sometimes accelerate development of an impending senile cataract.

A number of cases may require surgery because of postirradiation glaucoma.[9]

Postirradiation ocular carcinoma is a medical curiosity. Lane[24] reported 4 such cases following continued exposure to irradiation without protection.

RESULTS OF THERAPY

The results of all forms of treatment vary considerably. It is therefore difficult to evaluate the methods of treating neoplasms of the eyelids. In a series of cases studied for at least five years, Charteris[9] used radium needles and radon seeds interstitially in 76 cases and obtained excellent results. Sixty-eight cases were treated with one radium treatment. All were well or had died of other causes. Four cases receiving surgery in addition to radium were well. Two cases were well following the second course of radium therapy. Two cases were failures. Dollfus[12] in 100 cases used radium therapy in 96 cases, roentgen rays with radium in 3 cases and teleradium in 1 case. Eighty-eight patients were considered cured, 10 had complications in the eye or adnexa and were considered not cured. Two patients had extension of their lesions despite therapy. Laborde[23] treated 56 of 84 cases of epithelioma of the eyelid with radium. A cure was obtained in 50 cases. The other 28 cases were eliminated from this type of therapy because of perforation of the eyelids, invasion of the globe, or were treated with electrocautery and excision, and 4 cases would not submit to treatment. Benedict and Asbury,[1] in their series of 251 cases, treated 98 cases with radium. A few extensive inoperable lesions were included. There were 27 known recurrences. Of these, 12 lesions were advanced and the outlook was hopeless at the first examination. Eighty-seven cases had excision followed by radium, with 11 recurrences. Seven of them responded to further treatment. In 4 cases local recurrence did not occur but metastases developed. Twenty-nine cases had excision and cautery with no clinical recurrence as far as is known. Twenty-five cases had surgical diathermy, primarily, with recurrence in 4 of 7 cases of extensive tumor subjected to exenteration; 4 cases showed no recurrence. Two cases had diathermy and radium without recurrence. Seven had exenteration with no recurrence in 4 extensive tumors. Roentgen irradiation was given in 5 cases. The outcome is not known in 4 cases and there was no recurrence in 1 case. Driver and Cole[13] used various methods of treatment: radium, radon, and roentgen irradiation alone or in combination with surgery or surgery alone. Of 324 cases, 193 were followed from six months to ten years or more. There were 12 relapses (6.2 per cent) and 181 possible permanent cures (93.8 per cent). Seventy patients were observed longer than five years with 1 relapse, resulting in 98.3 per cent possible permanent cure. Of the 324 cases, there were 6 known

deaths from cancer. Birge,[2] using all methods of treatment, found that of 127 cases of basal cell carcinomas which were followed, 82 were living, 31 died of causes other than the epithelioma of the eyelid and 14 died from the effects of the epithelioma. Blindness occurred in 25.9 per cent. Smithers[34] using intermediate therapy with little or no filtration treated 57 patients with cancer of the eyelids. Of 39 primary cases, 3 required retreatment and all were cured. Of 37 patients alive and symptom free, 9 were observed more than two years, 10 from one to two years, 7 from six months to one year, and 11 for less than six months. In the group of 18 treated recurrences, 1 died six months later without healing, 4 recurred, 2 of these were retreated and became symptom free. Thirteen cases are alive and well without signs of growth. Braun[6] states that in Chaoul's series of 30 tumors of the eyelid, 29 responded satisfactorily and were essentially without symptoms. In his own series of 11 cases, in which all but 1 were deep-seated ulcerating tumors, Braun states that 6 were free of symptoms following treatment, 2 cases were partially successful and 3 cases were unsuccessful. Birge,[3] in treating 59 squamous cell carcinomas, graded his pathological material using Broders'[7,8] method. Lesions in Grade 1 were treated only with surgery, with no resultant deaths or loss of the eye. Death occurred in 15 per cent of the Grade 2 lesions and loss of the affected eye in 25 per cent of the cases. Recurrences were frequent and invasion of the orbit occurred in 30 per cent of the cases. Death occurred in 6 per cent of the Grade 3 lesions and loss of the affected eye in 53 per cent of the cases. There was recurrence with nearly all types of treatment. In 60 per cent of the cases the growth invaded the orbit and 40 per cent required exenteration. None of the persons with Grade 4 lesions survived five years, although 75 per cent were living three years after treatment. All of the patients lost the affected eye. Most of the cases in this series occurred in Grades 2 and 3. In 85 per cent of about 150 cases at the Memorial Hospital (New York) the first treatment was successful; 7 per cent required additional treatment. Only about 6 per cent died of the disease.[27]

This paper is a report of the results of treatment of 131 consecutive patients with 133 lesions of the eyelid seen in the Department of Radiology of the State University Hospitals, Iowa City, Iowa, from 1930 to 1943 inclusive. We believe that practically all recurrences will occur within three years following our initial treatment, therefore 31 lesions are excluded from the discussion because they have had inadequate study for the minimal three year period. Causes for inadequate study include (1) losing contact with the patient and (2) death from other causes occurring before the required lapse of time following the primary treatment.

Four general methods of irradiation were used, with some of the cases receiving surgery in combination with irradiation as the primary treatment. The earliest was by radium plaques. Ten lesions were treated in this manner. Various factors were used and doses in milligram hours were determined empirically. Eight lesions were followed three or more years. No interstitial radium and no radon in any form was used.

Fifteen lesions were treated using deep therapy, 200 kv., 8 and 20 ma., 40 to 50 cm. focus skin distance, Thoraeus filter (0.4 Sn, .25 Cu, 1.0 Al). Doses were fractionated and a total dose of 3,600 to 5,100 roentgens was given. The average dose was 4,500 r. Adequate study of 14 lesions was made.

The largest group—58 lesions—was treated by intermediate therapy at 100 to 135 kv., 5 ma., 0 to 3 mm. Al filter, 20 to 30 cm. focus skin distance. The total dose varied, the smaller doses of 800 to 2,000 r being given singly, while the larger doses, 2,000 to 5,000 r, were fractionated. Forty-one lesions were adequately studied.

Fifty lesions were treated using low voltage, short distance therapy. The tube was operated at 60 kv., 5 ma., 3 and 5 cm. focus skin distance, 0.2 mm. Cu inherent filtra-

tion with no added filtration. Single doses of 1,500 to 3,000 r were given to lesions measuring a few millimeters in size. Most treatments were, however, given in divided doses of 500 r daily, or 1,000 r every other day until a total dose of 6,000 to 7,000 r was given in ten to fourteen days. Thirty-nine lesions were studied three or more years. Using all types of treatment, 102 lesions were adequately surveyed for three or more years.

The results of treatment are divided into two groups. Group 1, "healed," includes all lesions having no residual or recurrent neoplasm for three or more years following the last treatment. Group 2, "not healed," includes all lesions which have not remained healed for three years following the last treatment.

The results of treatment of the 102 lesions were carefully studied. Eighty-seven (85.3 per cent) were healed, 15 (14.7 per cent) were not healed. Eight lesions were treated with radium plaques. Three (37.5 per cent) were healed and 5 (62.5 per cent) were not healed. Forty-one lesions were treated with intermediate therapy. Thirty-six (87.8 per cent) were healed and 5 (12.2 per cent) were not healed. Fourteen lesions received deep therapy. Twelve (85.7 per cent) were healed and 2 (14.3 per cent) were not healed. Thirty-nine lesions were treated using the low voltage, short distance therapy tube. Thirty-six (92.3 per cent) were healed and 3 (7.7 per cent) were not healed (Table v). From the study, the greatest percentage of healed lesions occurred in the group treated with low voltage, short distance therapy. Lesions treated with radium were the most difficult to control, with only 37.5 per cent healed. Deep therapy and intermediate therapy were slightly less effective than low voltage, short distance therapy, because we were unwilling to give as high dosage during the period when we were using deep and intermediate therapy as we now give with the low voltage, short distance therapy.

Seventy-two (70.6 per cent) of the 102 lesions were proved histopathologically. There were 54 basal cell, 10 squamous cell and 8 intermediate cell carcinomas. Forty-six (85.2 per cent) basal cell carcinomas were healed, 8 (14.8 per cent) were not healed. Eight (80.0 per cent) squamous cell carcinomas were healed and 2 (20.0 per cent) were not healed. Of the intermediate cell carcinomas 7 (87.5 per cent) were healed and 1 (12.5 per cent) was not healed (Table vi). The 30 lesions not having a histopathologic examination had an appearance typical of carcinoma and will be included in this discussion.

Driver and Cole[13] and Smithers[34] state that failure in effecting a cure was nearly twice as frequent in those patients who had previous treatment. At our initial questioning we found that 39 lesions had received previous treatment. The treatment consisted of (1) nonradiological and nonsurgical methods, such as ointments, patent medicines, caustics, ultraviolet light, acids, etc.; (2) surgical therapy alone, such as excision, cautery, surgical diathermy, etc.;

TABLE V

RESULTS FOLLOWING TREATMENT BY VARIOUS TECHNIQUES

Technique	Number of Lesions	Healed		Not Healed	
Radium	8	3	37.5%	5	62.5%
Intermediate roentgen therapy	41	36	87.8%	5	12.2%
Deep roentgen therapy	14	12	85.7%	2	14.3%
Low voltage, short distance roentgen therapy	39	36	92.3%	3	7.7%
TOTAL	102	87	85.3%	15	14.7%

TABLE VI

RESULTS OF HISTOPATHOLOGICALLY PROVED LESIONS

Method of Therapy		Basal Cell	Squamous Cell	Intermediate Cell	Total
Radium	Healed	2	0	0	2 28.6%
	Not healed	4	1	0	5 71.4%
Intermediate roentgen	Healed	15	3	1	19 86.4%
	Not healed	2	0	1	3 13.6%
Deep roentgen	Healed	11	1	2	14 93.3%
	Not healed	0	1	0	1 16.7%
Low voltage, short distance roentgen	Healed	18	4	4	26 92.9%
	Not healed	2	0	0	2 7.1%
TOTAL	Healed	46 85.2%	8 80.0%	7 87.5%	
	Not healed	8 14.8%	2 20.0%	1 12.5%	
		54	10	8	72

(3) surgery in combination with some form of irradiation; or (4) roentgen or radium therapy alone. The lesions previously treated with a nonradiological or nonsurgical method were all healed. The entire group which had previously received any form of treatment responded as well to irradiation as the entire group of 102 lesions.

Thirty-six lesions treated by us required additional treatment (Table VII). Further treatment included one or more of the following methods: radium; intermediate therapy; deep therapy; low voltage, short distance therapy, and some form of surgery —excision, enucleation, or radical operative procedures. Twenty-three (63.9 per cent) were healed and 13 (36.1 per cent) were not healed. Seven (87.5 per cent) of 8 lesions treated with radium initially received additional treatment, 2 (28.6 per cent) were healed, and 5 (71.4 per cent) were not healed. Twenty (48.8 per cent) of the 41 lesions treated initially with intermediate therapy received additional treatment, 15 (75.0 per cent) were healed and 5 (25.0 per cent) were not healed. Two (14.3 per cent) of 14 lesions treated with deep therapy received further therapy; both (100 per cent) were healed. Seven

TABLE VII

LESIONS RECEIVING ADDITIONAL RADIATION TREATMENT

Method of Therapy	Healed		Not Healed		Total	
Radium	2	28.6%	5	71.4%	7	87.5%
Intermediate roentgen	15	75.0%	5	25.0%	20	48.8%
Deep roentgen	2	100.0%	0	0.0%	2	14.3%
Low voltage, short distance roentgen	4	57.1%	3	42.9%	7	18.0%
TOTAL	23	63.9%	13	36.1%	36	35.3%
Final treatment, surgical	10	71.5%	4	28.5%		

(18.0 per cent) of 39 lesions treated with low voltage, short distance therapy received further therapy; 4 (57.1 per cent) were healed and 3 (42.8 per cent) were not healed. Lesions receiving additional treatment responded better if the lesion had first had either intermediate type therapy or deep therapy as the primary treatment. Lesions treated with the low voltage, short distance therapy responded less well and those treated with radium primarily responded poorly to additional treatment.

Fourteen of the lesions receiving additional treatment had in some cases associated with irradiation either excision, enucleation, or a more radical surgical procedure as the final treatment. Ten (71.5 per cent) were healed and 4 (28.5 per cent) were not healed. From these findings it is seen that 10 of the lesions responded to surgery and that therefore irradiation could not claim a cure. These lesions, however, are included in the discussion because they also had received irradiation in our department and we were able to delay the surgical procedure.

A total of 66 lesions receiving only a single treatment in our department (this includes those having had some form of treatment elsewhere) responded as follows: 63 lesions were healed, 3 were not healed. Our last examination of these 3 patients revealed residual neoplasm. They died without our knowledge of the condition of the lesion at the time of death.

The results of treatment depending on the location of the lesions about the eye are found in Table VIII. Lesions of the lateral canthus responded best while the lesions of the upper and lower lids responded the poorest.

Table VIII

RESULTS OF TREATMENT DEPENDING ON THE LOCATION

Location	Healed		Not Healed		Total	
Lower lid	47	82.4%	10	17.6%	57	55.9%
Upper lid	10	83.3%	2	16.7%	12	11.8%
Medial canthus	20	87.0%	3	13.0%	23	22.5%
Lateral canthus	9	90.0%	1	10.0%	10	9.8%
Total	86	84.3%	16	15.7%	102	

SUMMARY AND CONCLUSIONS

The results of the study of 133 epitheliomas of the eyelids treated in the Department of Radiology of the State University of Iowa Hospitals, Iowa City, Iowa, from 1930 to 1943 inclusive are as follows:

1. Eighty-seven lesions were studied histopathologically. Sixty-three (72.4 per cent) were basal cell, 13 (15.0 per cent) were squamous cell, and 11 (12.6 per cent) were intermediate cell carcinomas.

2. Anatomically, 133 lesions show the following distribution: lower lid, 73 (54.9 per cent); upper lid, 15 (11.3 per cent); medial canthus, 34 (25.6 per cent); lateral canthus, 11 (8.2 per cent).

3. Four general methods of irradiation were used: (a) radium therapy; (b) intermediate roentgen therapy using small single doses of 800 to 2,000 roentgens. With increase in experience, larger fractionated doses of 2,000 to 5,000 roentgens were given; (c) deep roentgen therapy was fractionated with a total dose of 3,600 to 5,100 roentgens given; (d) low voltage, short distance roentgen therapy with single doses of 1,500 to 3,000 roentgens given to small lesions. Larger lesions received fractionated doses of 6,000 to 7,000 roentgens.

4. Results following treatment of 102 lesions are as follows: (a) radium therapy, 8 lesions treated, 3 (37.5 per cent) healed; (b) intermediate roentgen therapy, 41 lesions treated, 35 (85.4 per cent) healed;

(c) deep roentgen therapy, 14 lesions treated, 12 (85.7 per cent) healed; (d) low voltage, short distance therapy, 39 lesions treated, 36 (92.3 per cent) healed.

Increase in experience resulted in increase in the total doses administered with resultant increase in the percentage of lesions healed. This is exemplified by the better percentage of healed lesions following low voltage, short distance therapy. We also believe that using low voltage, short distance therapy improved the cosmetic results and decreased the number of complications.

5. The group of lesions receiving previous treatment elsewhere responded as well to treatment as the entire group of 102 lesions. However, lesions treated by us that required additional treatment responded less well than the entire group of 102 lesions. The lesions receiving treatment by low voltage, short distance therapy responded less well to retreatment than those treated by intermediate therapy and deep therapy. Lesions treated by radium therapy responded poorly when retreated.

6. Sixty-six lesions received only a single course of treatment in our department. Sixty-three lesions remained healed.

7. Lesions of the lateral canthus responded best to treatment while lesions of the upper and lower lids responded less well.

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CHRONIC MASSIVE THROMBOSIS OF PULMONARY ARTERIES

A REPORT OF SEVEN CASES WITH CLINICAL AND NECROPSY STUDIES*

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THE clinical syndromes of *acute* obstruction in the pulmonary arteries by emboli or thrombosis and of *chronic* obstruction related to certain degenerative and inflammatory diseases of the heart, lungs, or pulmonary vessels are well known. There is a third type of pulmonary artery obstruction characterized by slowly developing thrombosis of the pulmonary arterial tree with progressive right ventricular failure. The latter clinical and pathological entity is the subject of this discussion.[4]

A brief review of the literature concerning this interesting and rare condition is pertinent. T. von Jurgensen[14] in Nothnagel's Practice (1908) stated that "when branches of the pulmonary artery are gradually occluded, a very large portion of the lumen may be rendered impermeable without causing death." He recognized that the failing heart was more likely than the normal to permit development of thrombi in the pulmonary artery. Barnes and Yater[1] in 1929 gave a clear-cut description of a case of chronic pulmonary thrombosis with congestive heart failure. Their patient was a man, aged thirty-four, who died of progressive myocardial failure five months after an episode of pulmonary embolism secondary to thrombophlebitis of the lower extremities. The electrocardiogram had shown right axis deviation. Autopsy revealed old thromboses in the main pulmonary artery and in both of its branches. These were evidently old. There was cor pulmonale.

Means and Mallory[10] in 1931 reported the case of a man, aged sixty, with right ventricular failure. The postmortem revealed complete thrombotic closure of the right pulmonary artery. In the periphery of the right lung were many arterial plugs, organized thrombi. Similar thrombi were found in the periphery of the left lung.

Brenner[2,3] made an exhaustive study of the pathology of the vessels of the pulmonary circulation and presented 7 cases of massive organized pulmonary arterial thrombi. He showed that thrombosis of the pulmonary arterial tree, if the smaller branches are included and minute thrombi sought, is common. In a series of 100 consecutive autopsies he was able on careful examination to demonstrate pulmonary arterial thrombi in 28 cases. Chronic massive thrombosis involving the main pulmonary artery or one of its branches is an uncommon occurrence, however, and it is seldom accurately recognized before death. Savacool and Charr[12] collected 88 such cases from the literature in 1941, adding twelve of their own.

Carroll[5] in 1950 reported 5 cases of massive obstruction of the major pulmonary arteries. He stressed cyanosis, dyspnea, orthopnea, polycythemia, right heart failure, and right axis deviation of the electrocardiogram. In the roentgenogram he pointed out prominence of the pulmonary arteries and clear lung fields as the result of pulmonary obstruction. In 1 instance he demonstrated the obstruction by means of angiocardiography, and in 2 cases he showed elevation of pressure in the right ventricle and pulmonary artery on cardiac catheterization. Hanelin and Eyler[6] in a recent publication, stressed the roentgenographic findings in pulmonary thrombosis and also emphasized the development of

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cor pulmonale and right heart failure in cases of long duration.

ETIOLOGY AND ASSOCIATED PATHOLOGIC CHANGES

Pathogenesis in a proved case of pulmonary thrombosis may be difficult or impossible to establish. Brenner concluded from his studies that most thrombi of the pulmonary arteries are embolic in origin, the emboli originating in the systemic veins or right heart. This sequence can be recognized in only one patient of the present series (Case VII). Local development of the thrombus is also a frequent occurrence. Numerous case reports in the literature illustrate that various pulmonary, cardiac and pulmonary vascular diseases may result in local thrombus formation in the pulmonary artery and its branches. These have been reviewed in a recent publication,[6] and they may be classified generally in two categories: (1) that in which primary lung disease, such as infection or tumor, directly involves the pulmonary arterial tree and leads to pulmonary thrombosis with propagation of the clot (Case II); (2) the group characterized by diffuse vascular disease of the lungs, usually secondary to degenerative or chronic inflammatory disease, or secondary to mitral stenosis, but occasionally the result of a primary vascular inflammatory process. Here the following events occur: (a) pulmonary hypertension (b) hypertrophy of the right ventricle; (c) right heart failure; (d) thrombosis of the pulmonary artery, which aggravates the existing disease and results in sudden death.

Apparently, patients who have had pulmonary emboli, and those suspected of primary cor pulmonale from whatever cause, are those most likely to develop pulmonary thrombosis. In the series of Kampmeier[9] there were 3 patients with mitral stenosis. Pou and Charr[11] reported 6 cases of antemortem thrombosis of the pulmonary artery among 150 consecutive autopsies over a three year period. One hundred and five of these patients had far advanced pulmonary tuberculosis, 45 silicosis. The series of Savacool and Charr consisted of 12 autopsied cases, all having pulmonary tuberculosis.

The *symptoms* of pulmonary artery thrombosis are often those of ordinary congestive failure. Associated pulmonary disease will often be apparent. The diagnosis of thrombosis, therefore, is seldom made before death, the formation of thrombi usually being unsuspected. The duration of symptoms dating from the onset of thrombosis or embolism may be as short as two weeks or as long as four years.[13] The occurrence of thrombi is commonest in the older age groups, but instances have been reported in children,[7] and, in the presence of antecedent emboli, chronic massive thrombosis may occur at any age. Cyanosis may or may not be present, although it is sometimes severe. In the series of Johnson,[8] which included 43 autopsied cases, labored dyspnea, tachypnea, increased pulse, increased respiration, cyanosis and collapse were the leading symptoms, and 9 patients had symptoms so atypical that the diagnosis was considered impossible even in retrospect. Pulmonary infarction or embolism is not a necessary part of the clinical or pathologic picture, though it may occur if fragments of the thrombi become detached to migrate peripherally in the smaller branches of the pulmonary arteries; embolism of the lung may characterize the clinical onset.

ROENTGENOGRAPHIC ASPECTS

Westermark[16] has completely described alterations in the roentgen appearance of the chest resulting from pulmonary embolism, thrombosis and infarction. Of specific interest are those changes which result from ischemia of the lung peripheral to the intravascular occlusion, manifested by diminished vessel markings in the parts of the lung fields supplied by the affected arterial branches. These peripheral vessels are contracted and relatively devoid of blood distal to the point of obstruction. They are small in size and reduced in visible number, producing the net roent-

TABLE I

SUMMARY OF SEVEN CASES OF PULMONARY ARTERY THROMBOSIS

Case Number	Age	Associated Condition	Arteries Thrombosed	Microscopic Diagnosis
I	54	Chronic alcoholism; vitamin deficiency	All main branches of right pulmonary artery	Pulmonary arteriosclerosis and arteriolar sclerosis. Diffuse proliferative endarteritis
II	63	Chronic pulmonary emphysema, slight. Patent interauricular septum; old myocardial infarct	Main pulmonary artery and all large branches	Pulmonary arteriosclerosis. Focal chronic pulmonary arteritis, tuberculous
III	73	Pulmonary emphysema, marked. Bronchitis and bronchiectasis	Main pulmonary artery, right and left pulmonary arteries, and branches to left lower lobe, right middle and lower lobes	Pulmonary arteriosclerosis and arteritis, focal
IV	56	Adenocarcinoma of the stomach	Right main branch of pulmonary artery and many smaller branches bilaterally	Pulmonary arteriosclerosis
V	75	Chronic pulmonary emphysema, slight	All main branches of pulmonary artery	Pulmonary arteriosclerosis and arteriolar sclerosis, characterized by intimal thickening. Arteritis, focal, with medial infiltration by lymphocytes
VI	46	Chronic pulmonary emphysema, slight	Both main branches of pulmonary artery, and medium branches of right and left pulmonary artery	Pulmonary arteriosclerosis and arteriolar sclerosis, slight. Mesarteritis and periarteritis of the pulmonary artery, marked, with necrosis of intima and destruction of the elastic fibers
VII	67	Carcinoma of the prostate; pulmonary emphysema, mild	Right main branch of pulmonary artery; lower lobe branches of left pulmonary artery	Pulmonary arteriosclerosis, slight

genographic effect of segmental blackening of the lung fields.

In the event of embolism or thrombosis involving a major branch, the affected vessels will often be enlarged at the point of obstruction and dilated proximally to it in a manner to provide a clue to the pathologic process involved. At the same time, the roentgenographic appearance of pulmonary infarction may occur. In patients who survive a sufficiently long period, it may prove possible to observe progressive enlargement of the hilar arteries and progressive simultaneous blackening of the lung fields due to ischemia. These changes in the appearance of the lung fields are often subtle. In addition, the large hilar arteries may become more sharply outlined because they no longer possess intrinsic pulsations, at times resembling large lymph nodes.

Seven clinical cases of pulmonary artery thrombosis have been seen and were examined postmortem. Table I is a summary of the cases.

REPORT OF CASES

CASE I. This fifty-four year old female gave a history of chronic alcoholism for at least four

years. Her diet was inadequate. Progressive fatigue and dyspnea on effort had been noted for two years. No cause other than her vitamin deficiency could be found. Signs of congestive failure developed, with hydrothorax and ascites. The blood pressure was 118/96. No murmurs were heard. Significant laboratory data are tabulated (Table III). The electrocardiogram showed evidence of right ventricular hypertrophy, with tall R waves across the precordium (Fig. 1). A chest roentgenogram made shortly after her first admission to the hospital revealed mild cardiac enlargement and no evidence of heart failure (Fig. 2). On one occasion the pleural fluid culture was reported as showing tubercle bacilli. The patient improved after bed rest, salt restriction, digitalization, and mercurial diuretics. She received streptomycin. A well balanced diet and vitamin therapy were included. An attack of varicella was followed by increase in the severity of the

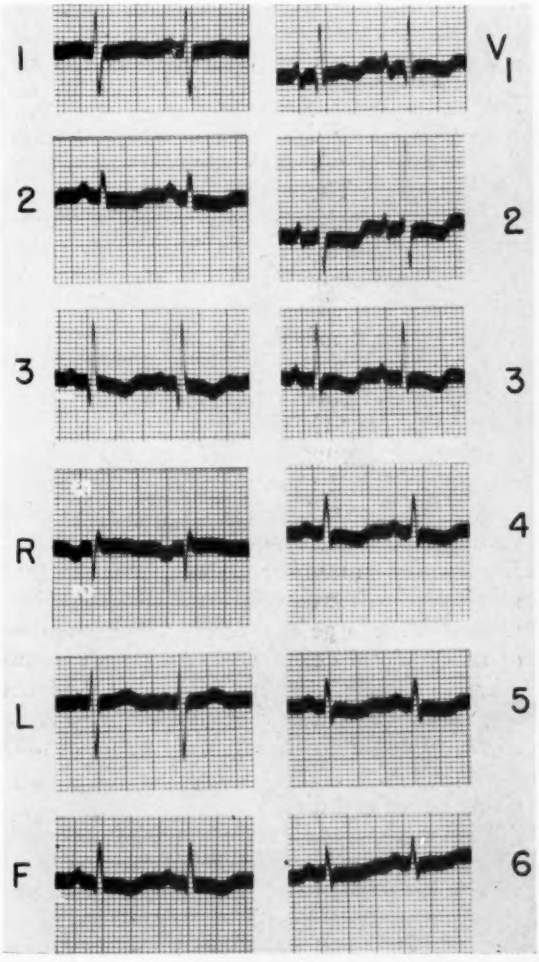

Fig. 1. Case 1.

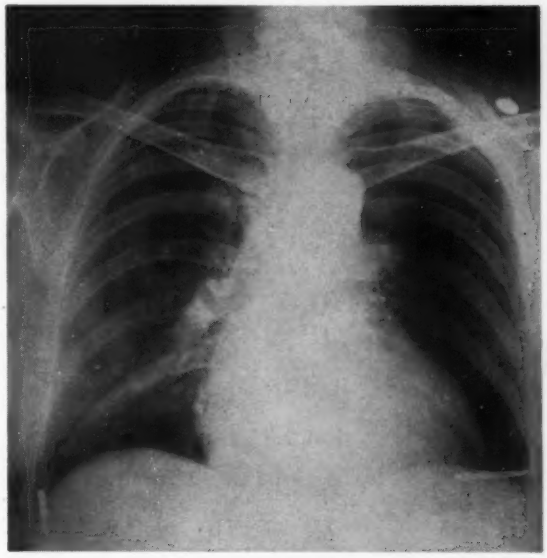

Fig. 2. Case 1. Roentgenogram made one year before death. Mild cardiac enlargement. Left main branch of pulmonary artery is prominent. Peripheral vessels inconspicuous. No evidence of heart failure.

Fig. 3. Case 1. Chest roentgenogram made a few days before death. Left branch of pulmonary artery now more prominent. Heart has not increased in size. Peripheral vessel shadows normal or slightly reduced in size and number. Accumulation of pleural fluid on right.

symptoms, and further therapy was ineffectual. Cyanosis and dyspnea at this time were increased. Three weeks before death, marked distention of the neck veins, free peritoneal

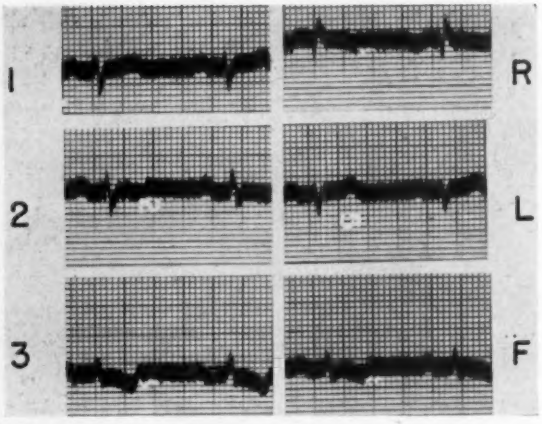

FIG. 4. Case II.

fluid and edema of the extremities developed. She was markedly cyanotic, and a presystolic murmur was heard. Roentgenoscopic and roentgenographic studies of the chest made a few days before death revealed cardiac pulsations of diminished amplitude. There was a small volume of free pleural fluid on the right, but no evidence of passive congestion (Fig. 3).

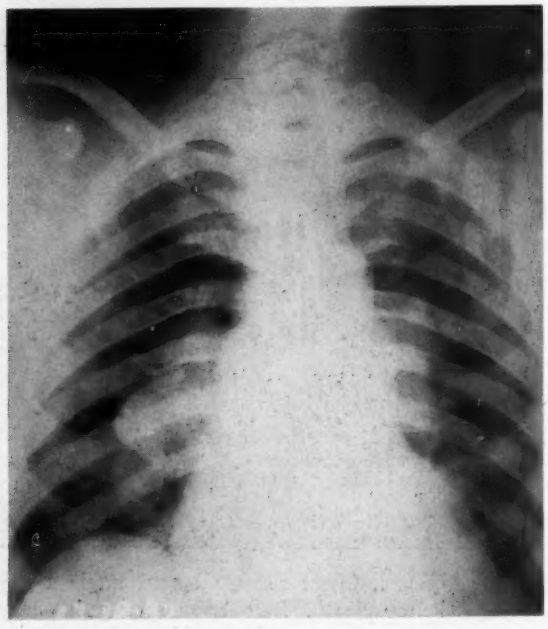

FIG. 5. Case II. Roentgenogram about one year before death. Heart enlarged, pulmonary arteries massive, well delineated, comma shaped. Note calcium deposit visible in one of the right main pulmonary arterial branches in the right hilus. The relatively small size and number of the peripheral vessels is out of proportion with the main pulmonary arterial branches, which are huge.

The diagnoses considered were (1) beri beri heart disease, (2) pulmonary arterial disease, (3) pericardial compression due to tuberculosis.

The postmortem examination revealed cor pulmonale (heart weight 530 gm.) with organized thrombi of large and small arteries of both lungs and an infarct of the right lower lobe. The thrombi to the right upper and middle lobes were pale gray. The thrombus in the artery to the right lower lobe was reddish brown, and was obviously more recent than the other thrombi. The veins of the legs were exposed and no thrombi were found. Microscopic sections revealed hypertrophy of the right ventricle. Some of the smaller arteries of the lungs were obliterated by old organizing thrombi. The lung vessels showed evidence of exudative and proliferative endarteritis.

In summary, this patient had cor pulmonale incident to diffuse arteriolar disease, with thrombosis of many large pulmonary vessels. The signs were those of chronic congestive heart failure.

CASE II. This sixty-three year old male was known to have hypertension for three years, with progressive dyspnea, enlargement of the liver and pedal edema. The heart was considerably enlarged. There was a systolic murmur at the apex and a high-pitched diastolic murmur over the pulmonic area. The blood pressure was 132/88. Significant laboratory data are tabulated (Table III). The electrocardiogram showed abnormal right axis deviation with inverted T in leads 2 and 3 (Fig. 4). The chest leads did not show abnormally tall R waves across the precordium, but the T waves were all inverted. A chest roentgenogram made on admission to the hospital had shown moderate cardiac enlargement, huge pulmonary arteries, and peripheral vessels which were relatively small in size and few in number. Subsequent roentgenoscopic study showed minimal amplitude of pusations in the large hilar arteries. The possibility of atrial septal defect was considered, despite the lack of hilar activity (Fig. 5). Shortly before death a chest roentgenogram revealed slight increase in heart size, but no other change (Fig. 6). The patient became progressively worse and died.

Pathologic examination revealed a hemorrhagic infarct of the left lobe of the cerebellum with subarachnoid and intraventricular hemorrhage; organized hyalinized thrombus of the main primary and secondary branches of both pulmonary arteries, with focal calcification of

the thrombus and wall of the right pulmonary artery near a calcified tuberculous focus in a lymph node. There were old myocardial infarcts of both ventricles of the heart, an organized mural thrombus of the right ventricle, hypertrophy of the heart (800 gm.); patent foramen ovale, and an infarct of the upper lobe of the right lung.

In summary, this man died suddenly in chronic congestive failure. Massive pulmonary arterial thrombi were found at autopsy. The massive character of the occlusion suggested an embolic origin, with possible sources leg varicosities and a mural thrombus of the right ventricle. The possibility of tuberculous arteritis as the cause of formation of the thrombi was also considered.

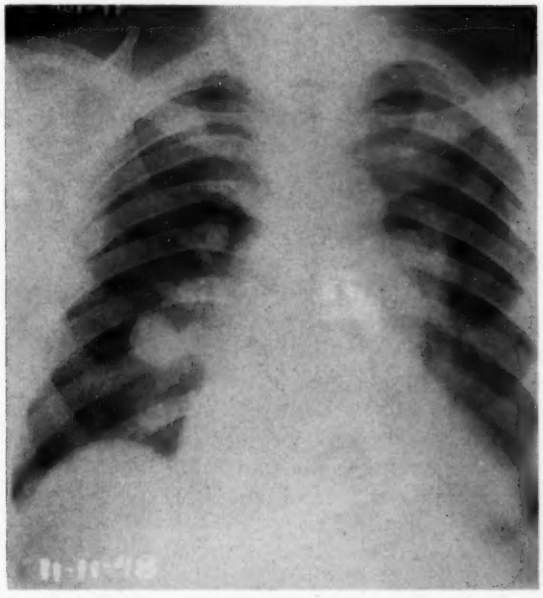

Fig. 6. Case II. Roentgenogram made shortly before death. Enlarged heart has increased slightly in size. Main branches of pulmonary artery unchanged. Peripheral vessels adjacent to left hilus now comparatively diminished in size and number.

Case III. This seventy-three year old man gave a history of paroxysmal nocturnal dyspnea of two months' duration prior to admission to the hospital. He had edema of the legs, an en-

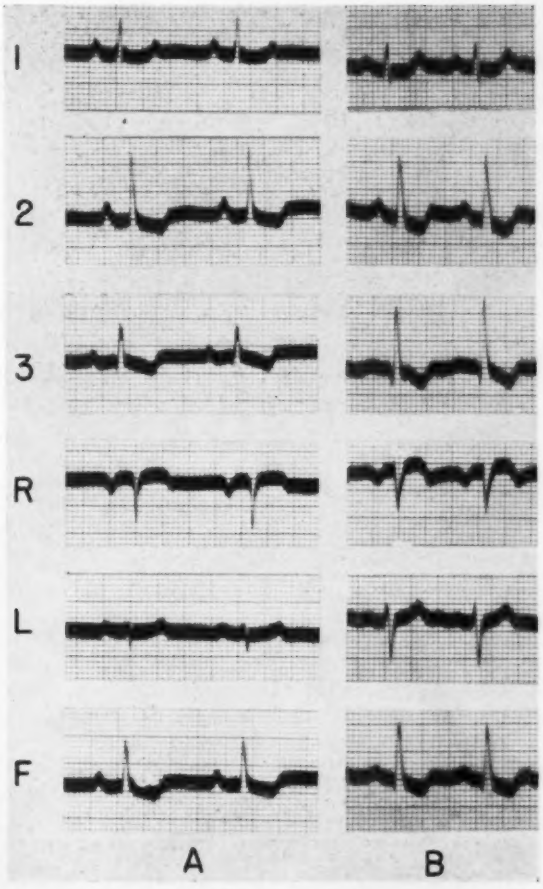

Fig. 7. Case III.

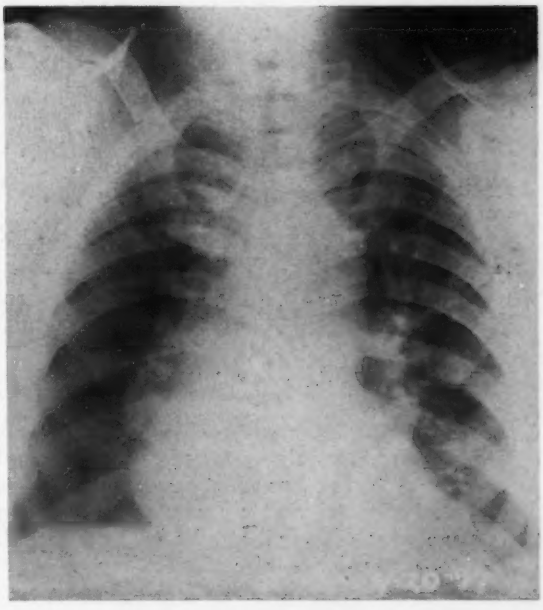

Fig. 8. Case III. Roentgenogram made five weeks before death. Heart moderately enlarged, large pulmonary arteries, rounded at inferior margins in hilar regions. Peripheral vessels not diminished in size or number. There is no gross vascular congestion of the lungs, although a mild degree of passive hyperemia may exist.

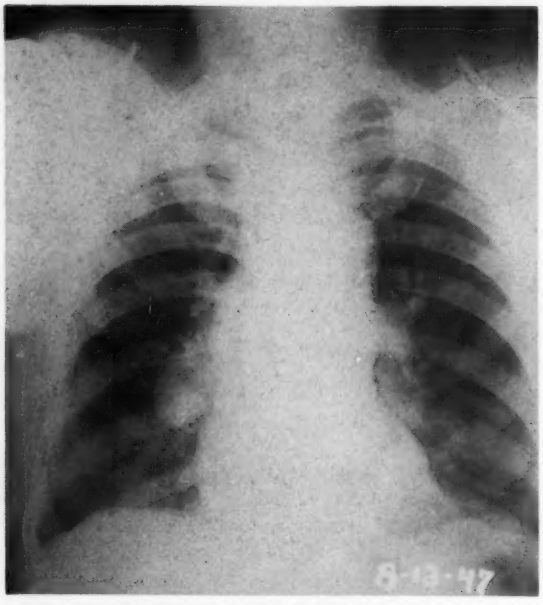

FIG. 9. Case III. Roentgenogram made three weeks before death. Heart shadow now much smaller following treatment of congestive failure. Hilar arteries massive and sharply circumscribed. Peripheral vessels normal in appearance.

FIG. 10. Case III. Roentgenogram made three days before death. Heart now a little larger. Pleural fluid collecting at left lung base. Hilar masses persist. Peripheral vessels appear less prominent in some areas of lung fields. No evidence of pulmonary congestion despite enlarged heart.

larged liver, and dyspnea. The blood pressure was 172/105. The heart was enlarged. No murmurs were heard. Significant laboratory data are tabulated (Table III). The first electrocardiogram (Fig. 7*A*) on August 5, 1947, showed sinus rhythm, pulmonale P waves, and tall R waves across the chest. The electrocardiogram taken on September 5, 1947 (Fig. 7*B*) shows a shift of the electrical axis to the right. A chest roentgenogram on admission revealed an enlarged heart. There were bilateral hilar masses (Fig. 8). The patient improved after digitalization and diuretics, and the blood pressure returned to normal. Roentgenoscopic and roentgenographic studies of the chest at this time showed no apparent intrinsic pulsations of the hilar masses, which were thought possibly to represent enlarged lymph nodes. The lung fields were now a little clearer and the heart smaller (Fig. 9). A relapse soon occurred, with a severe cough productive of brownish sputum. A chest roentgenogram made three days before death revealed pneumonia or infarction at the base of the left lung. The heart had again increased in size (Fig. 10). The patient died suddenly. Autopsy revealed the heart to be hypertrophied, especially the right ventricle. Firmly attached to the wall of each main pulmonary arterial branch was a gray and yellow thrombus. Chronic pulmonary emphysema and bronchitis were noted.

In summary, this patient survived three months following onset of chronic congestive failure. Cor pulmonale was due to pulmonary emphysema, chronic bronchitis, and focal pulmonary arteritis.

CASE IV. This fifty-six year old man was admitted to the hospital complaining of dyspnea and cough of one and one-half years' duration, and edema of the feet, anorexia, weight loss, weakness, and epigastric pain for five months. Nausea was felt one month before admission. The patient was prematurely old. The heart was slightly enlarged to the left. The blood pressure was 150/100. Significant laboratory data are tabulated (Table III). The electrocardiogram showed sinus rhythm, inversion of T in leads 2 and 3, and the T wave in V_4 was sharply negative. A chest roentgenogram confirmed the presence of moderate cardiac enlargement, with no particular prominence of the right ventricular contour. The right main branch of the pulmonary artery was large, tapering to a point

in the lower hilar region. There was no pulmonary congestion (Fig. 11). Gastrointestinal examination revealed gastric carcinoma, and a gastric resection was performed on the twentieth hospital day. The patient died on the first postoperative day. The specimen showed ulcerative adenocarcinoma.

Autopsy revealed chronic arteritis of the small branches of the pulmonary artery with many recent and partially organized thrombi. The right main pulmonary artery was filled by a large pink and yellow thrombus. Many of the smaller branches of both lungs were thrombosed. The heart was slightly enlarged, especially the right ventricle. There were thrombi in the apex of the right ventricle.

In summary, this patient with a carcinoma of the stomach suffered from circulatory embarrassment of five months' duration. The embolus or thrombus of the main right pulmonary artery and thrombosis of smaller vessels may have been the immediate cause of death.

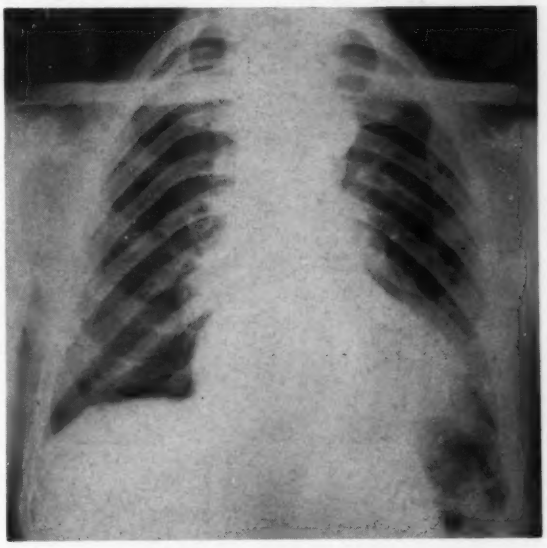

Fig. 11. Case iv. Roentgenogram made two weeks before death. Heart moderately enlarged. Right branch of pulmonary artery prominent, tapering sharply at lower margin.

Case v. This sixty-five year old male was admitted to the hospital because of chest pain and dyspnea of four weeks' duration. Physical examination revealed no cardiac enlargement, pulmonary emphysema, and a soft blowing systolic murmur at the apex. Blood pressure was 110/80. Significant laboratory data are tabulated (Table iii). The electrocardiogram showed sinus rhythm, rate 88 per minute. There was an S wave in lead 1 and inverted T waves in CR_2 and CR_4. The small R waves in CR_4 suggested clockwise rotation of the heart. Roentgenoscopic and roentgenographic studies of the chest revealed that both hilar shadows were more prominent than usual. They did not pulsate actively. The heart was slightly enlarged. The peripheral vessels in general were inconspicuous, especially throughout the right lung field (Fig. 12). On the fourth hospital day, following pyelography, the patient suddenly went into shock and died quickly. Postmortem examination revealed the heart to be somewhat hypertrophied, especially the right ventricle (weight 410 gm.), with marked arteriosclerosis and arteriolosclerosis of the pulmonary arterial tree. There were thromboses of all main branches of the pulmonary artery. An old infarct of the left lung was described. Emphysema was present.

In summary, this patient with chronic emphysema and pulmonary arteriosclerosis had old thrombi blocking all major pulmonary arteries. There was right ventricular hypertrophy. The sudden death may have been caused by the pulmonary arterial disease or by the injection of diodrast.

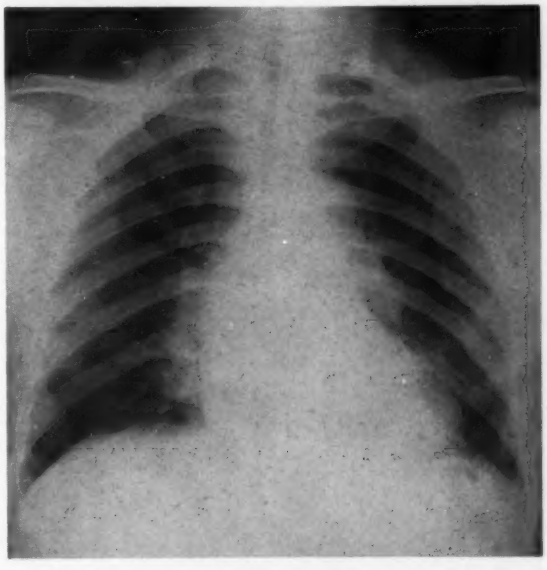

Fig. 12. Case v. Roentgenogram made three days before death. Mild cardiac enlargement. Pulmonary arteries prominent. Peripheral vessels variable in size and number, but generally inconspicuous. Pulmonary emphysema.

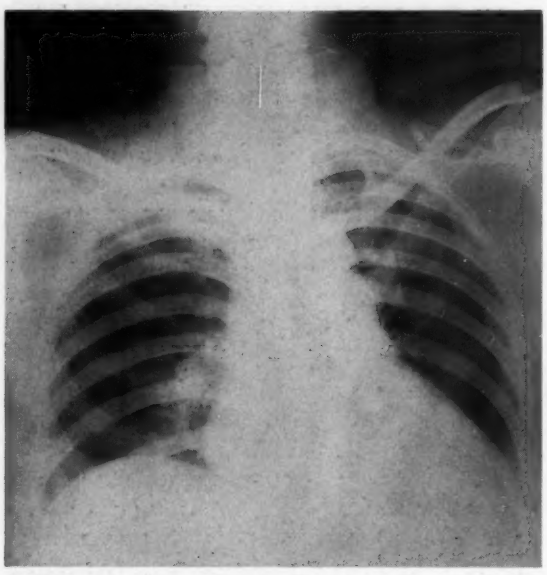

FIG. 13. Case VI. Roentgenogram made twenty-four hours before death. Heart enlarged to left. Both main branches of the pulmonary artery are prominent. Note clarity of left mid-lung field.

CASE VI. This forty-six year old female gave a history of dyspnea on exertion for two years. She was forced to give up her housework six months previously. Paroxysmal nocturnal dyspnea began about this time. The patient became increasingly dyspneic two months before admission. Periods of unconsciousness occurred and a cough, productive of blood-streaked sputum appeared. On physical examination the patient was in acute respiratory distress. The heart was enlarged. There was a systolic murmur at the apex. The liver was palpable. The blood pressure was 110/90. A chest roentgenogram showed moderate cardiac enlargement. The main branches of the pulmonary artery were large. The peripheral vessels were variable in size and number, but diminished in both respects on the left (Fig. 13). Seven hours after admission the patient suddenly became much more dyspneic and was intensely cyanotic. Frothy pink sputum appeared. Moist rales were heard over the entire pulmonum. Therapy included oxygen inhalation and morphine. Death occurred thirty minutes later. The clinical diagnosis was rheumatic heart disease and possibly pulmonary infarction.

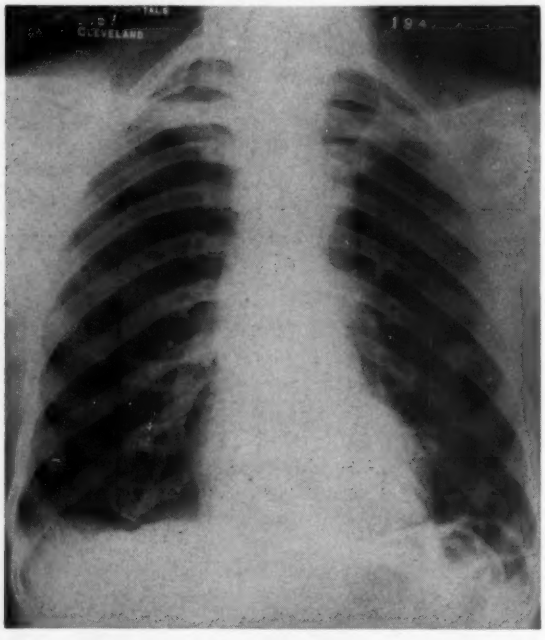

FIG. 14. Case VII. Control roentgenogram before operation. Heart and hilar shadows normal. Pulmonary emphysema.

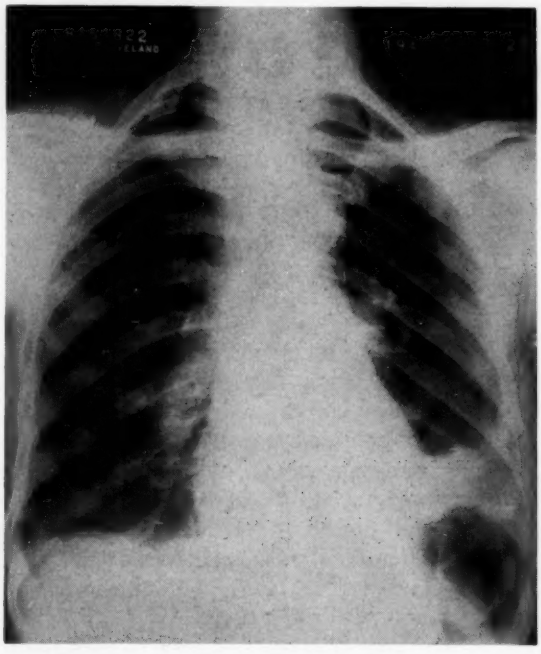

FIG. 15. Case VII. Hilar vessels have increased in size and the peripheral lung shadows are less conspicuous than they were before operation. Abnormal shadows at left lung base are the result of pulmonary infarction.

Postmortem examination showed organized thrombi of right and left pulmonary arteries,

hypertrophy and dilatation of the heart, especially of the right ventricle (weight 390 gm.), mural thrombi of the right atrium and right ventricle, severe arteriosclerosis of the coronary arteries with focal stenosis, organized thrombi of medium branches of the pulmonary arteries, and chronic plumonary emphysema. Microscopic examination showed mesarteritis and periarteritis of the pulmonary artery.

In summary, this patient had been disabled by dyspnea for six months. Cor pulmonale may have resulted from pulmonary arteritis, the thrombi in the pulmonary circulation resulting finally in acute heart failure.

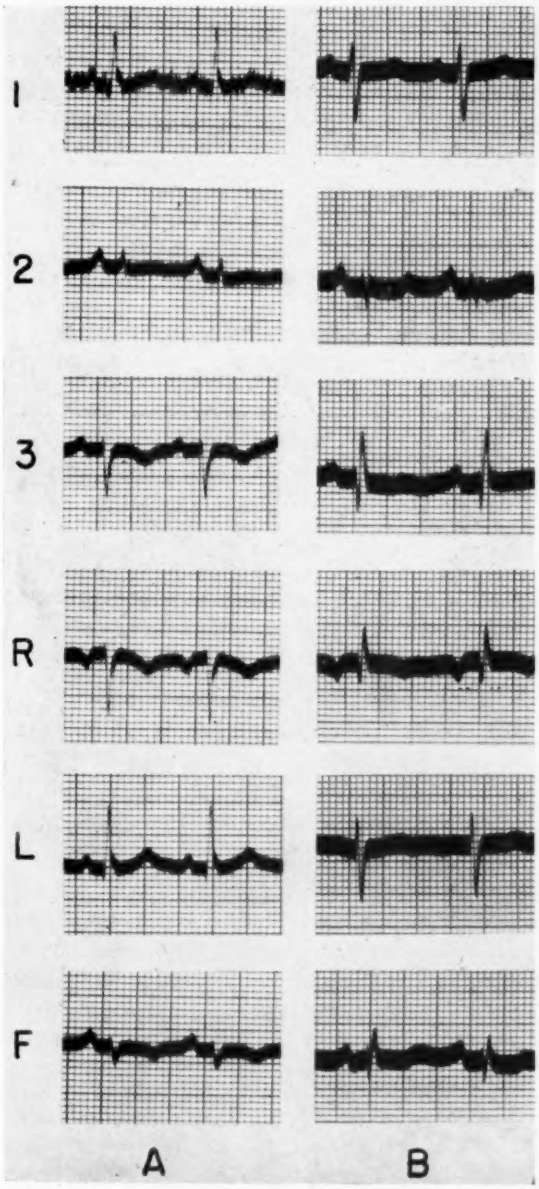

Fig. 16. Case vii.

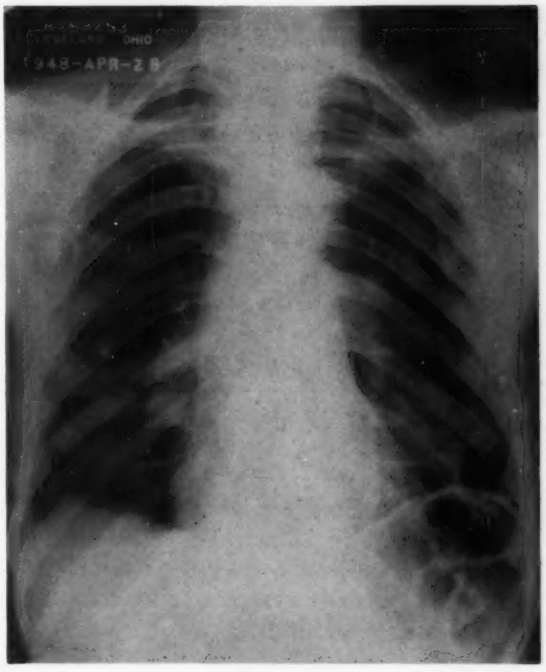

Fig. 17. Case vii. Roentgenogram made one week before death, nine months after postoperative embolism. Right main branch of pulmonary artery now massive and pointed at inferior margin. Lung fields abnormally clear, especially the right.

Case vii. This sixty-six year old man had a transurethral resection of the prostate on September 2, 1947. Histopathological examination showed carcinoma. A preoperative chest roentgenogram revealed no abnormality (Fig. 14). During the postoperative period the patient had fever. Chest films at this time revealed changes consistent with pulmonary infarction (Fig. 15). The electrocardiogram (Fig. 16*A*) showed left axis deviation and pulmonale P waves. The patient was readmitted to the hospital eight months later because of severe dyspnea, cough and ankle edema. Digitalis and mercurial diuretics relieved him. The blood pressure was 145/90. The heart was not demonstrably enlarged. A diastolic murmur was now heard over the pulmonic area. There was striking clubbing of the fingers. A chest roentgenogram made a few days before death revealed progressive changes characteristic of pulmonary thrombosis (Fig. 17). The electrocardiogram (Fig. 16*B*) now showed a remarkable

change—right axis deviation and inverted T waves in 1, 2, and 3 and V_1 to V_6. The P waves were tall and peaked. Laboratory data are tabulated (Table III). Death occurred thirteen days after the final hospital admission, eight months after the episode of pulmonary embolism.

Postmortem examination showed a hypertrophied heart (410 gm.), chiefly of the right ventricle. The right pulmonary artery was completely occluded by a laminated, reddish brown and yellowish gray, firmly adherent thrombus which distended the pulmonary artery to 5 cm. in diameter and extended from the bifurcation of the artery to the middle portion of the right lower lobe. The branches of the left pulmonary artery to the left lower lobe were occluded at their origin. The pulmonary arteries showed slight arteriosclerotic change. There was chronic pulmonary emphysema.

Summary. This is evidently a case of subacute cor pulmonale, in which the initial episode (pulmonary embolism) occurred eight months before death, a portion of the embolus lodging in the main pulmonary branches to organize, propagate slowly, and result eventually in death.

DISCUSSION

The clinical and laboratory data of the present series are summarized in Tables II and III. It is of interest that cyanosis and polycythemia were uncommon, despite severe and prolonged pulmonary obstruction. Dyspnea was present in all cases, sometimes severe, and death was always sudden and unexpected. The double-peak arm to tongue circulation time in Case II was evidently the result of a functional patent foramen ovale.

Electrocardiographic Findings. Electro-

TABLE II

CLINICAL FINDINGS

Case	Dyspnea	Cyanosis	Congestive Failure	Duration of Symptoms	Blood Pressure	Mode of Death
I	+	+	+	1yr.	118/96	Sudden
II	+	−	+	4 yr.	132/88	Sudden
III	+	−	+	2 mo.	160/100	Sudden
IV	+	−	−	1 yr. 7 mo.	140/70	Sudden
V	+	−	−	1 yr.	110/80	Sudden
VI	+	Terminal	+	2 yr.	110/90	Sudden
VII	+	−	−	8 mo.	142/90	Sudden

TABLE III

LABORATORY FINDINGS

Case	Red Blood Cell Count (millions)	Hemoglobin (%)	Venous Pressure Saline (mm.)	Vital Capacity (cc.)	Circulation Times Seconds Arm-Lung (Ether)	Arm-Tongue (Magnesium sulfate)	Electrocardiogram
I	4.2	82	200	1900	5.5	23	Right ventricular hypertrophy
II	6.0	103	150	1200	8.0	10 and 25 (double peak)	Right ventricular hypertrophy
III	4.5	84	180	2900	17	22	Right ventricular hypertrophy
IV	3.8	55	*	*	*	*	Deep S_1
V	3.3	80	*	*	*	*	Right ventricular hypertrophy
VI	5.24	109	*	*	*	*	No record
VII	5.3	90	*	*	*	*	Right ventricular hypertrophy

cardiograms were taken of 6 of the 7 patients after the onset of symptoms leading to death. In 4 cases electrocardiograms were taken six months (I), eleven months (II), two months (III), and nine months (VII) before the final electrocardiogram. In 3 of the 4 cases the early and late electrocardiograms were strikingly similar. In 1 case (Fig. 16, Case VII) the early record showed abnormal left axis deviation ($-64°$) whereas the late electrocardiogram showed abnormal right axis deviation ($+150°$). The electrocardiogram showed normal sinus rhythm in all cases. Pulmonale P waves were present in 3 of the 6 cases in which an electrocardiogram was taken. In Case II, the P waves were broad and notched. The voltage of the limb leads was in the lower limits of normal in all instances. The mean electrical axis in the 6 cases varied between $+65°$ and $+150°$, with an average of $+99°$.

Roentgenographic Diagnosis. When control and progress roentgenograms are available, the radiologist may be able to arrive at the correct diagnosis independently. However, it is seldom that this ideal sequence occurs, as it did in Case VII. The principal barrier to accurate roentgenographic diagnosis of this relatively rare condition is the common association of cor pulmonale, with enlarged pulmonary arteries, and pulmonary emphysema, the latter simulating the much less common pulmonary ischemia. When pulmonary thrombosis occurs as a complication, the additional changes may prove too subtle for recognition, except in retrospect.

Care is required to separate the changes due to pulmonary thrombosis from other disease manifestations. For example, enlarged lymph nodes may present a diagnostic problem. The tapering effect inferiorly, as described in the illustrations, is characteristic of the pulmonary arteries as their descending branches diminish in caliber inferiorly. In most instances, this feature will serve to distinguish arteries from other structures, in addition to their expected location. One must also differentiate an abnormal hilar mass with segmental emphysema (bronchogenic carcinoma) from an abnormal hilar mass with segmental ischemia (thrombosis). Other causes of pulmonary artery enlargement, such as congenital heart disease, need be mentioned only in passing.

CONCLUSIONS

The syndrome of chronic massive thrombosis of the pulmonary arteries is characterized by chronic congestive heart failure, refractory as a rule to the usual therapy. Cyanosis and clubbing may be present. Murmurs are frequently lacking. The electrocardiogram shows a tendency to right axis deviation, and a change from left to right axis deviation may be observed over a period of months. Roentgenographic changes to be searched for are progressive enlargement of the pulmonary artery with simultaneous signs of pulmonary ischemia, segmental or total. (It should be emphasized that congestive failure is typically of the right heart.) The diagnosis is to be considered when the syndrome of right heart failure occurs without pulmonary congestion, indicating that obstruction exists in the lesser circulation.[15]

SUMMARY

Chronic massive thrombosis of the pulmonary artery is a clinical entity characterized by:

1. Chronic congestive heart failure without passive congestion of the lungs.
2. Electrocardiographic findings of right ventricular hypertrophy or change by serial records from left to right axis deviation.
3. Enlarged pulmonary arteries and abnormally radiable lung fields as the result of pulmonary thrombosis and pulmonary ischemia respectively.
4. A subacute course with relatively mild symptoms leading to sudden death.

Seven cases illustrating this uncommon syndrome have been presented.

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Vol. 69, No. 2

MYELOGRAPHIC DEMONSTRATION OF SPINAL CORD METASTASES FROM PRIMARY BRAIN TUMORS*

By ERNEST H. WOOD, M.D., JUAN M. TAVERAS, M.D., *and* J. LAWRENCE POOL, M.D.

WHILE metastasis of primary cerebral and cerebellar tumors to organs outside of the nervous system is rare, there is increasing evidence that metastasis or spread of brain tumors to other portions of the nervous system by way of the cerebrospinal fluid circulation is a relatively common occurrence. The major evidence for such metastases thus far has been postmortem examination or surgical exploration for spinal cord decompression. The value of myelography for detecting spinal metastases from primary brain tumors and for determining the effect of roentgen therapy upon the metastatic lesions will be discussed in this paper.

PATHOLOGY

The extension of a cerebellar tumor to the spinal cord was described over a century ago by Ollivier[11] (1837). Since this time the discussion of metastatic gliomas of the spinal cord, particularly metastasis from cerebellar medulloblastomas and posterior fossa ependymomas, has been carried on by numerous authors including Spiller[12] (1907), Lahmeyer[6] (1913), Gordinier and Sawyer[4] (1911), and others more recently. The frequent occurrence of spinal cord metastases from medulloblastoma of the cerebellum is now so well recognized that patients receive routine radiation therapy to the spine at the time the primary tumor is irradiated. The frequency of occurrence of spinal metastasis from other types of brain tumor has been emphasized by Cairns and Russell[1] (1931). On examining the spinal cords of a group of patients with cerebral gliomas, these authors found gross evidence of spinal metastases in more than one-third of the cases. More than one-half of the cerebral gliomas which metastasized to the spinal cord were not medulloblastomas but tumors classified as glioblastoma multiforme, astrocytoma, ependymoma, neuroepithelioma and one unidentified glioma of the third ventricle. Moreover, an almost equal number of these primary tumors originated in portions of the brain above the tentorium as in the cerebellum and fourth ventricle.

Spinal metastasis from brain tumor constitutes 4 per cent of all spinal cord neoplasms, in the experience of Wolf.[15] The figure places the lesion fifth in frequency in the relative incidence of spinal cord tumors behind neurinoma, meningioma, metastatic carcinoma and primary glioma. The low incidence of spinal metastasis so frequently reported in other series is explained as resulting from infrequent routine examination of the spinal cord at necropsy.

On gross pathologic examination of the spinal cord two types of glioma metastases may be found. The more common type of involvement is the presence of discrete nodular implants upon the spinal cord and spinal nerve roots (Fig. 1). Usually more lesions are found on the dorsal aspect of the spinal cord than elsewhere, and the individual nodules, varying from microscopic size to several centimeters in diameter, are usually grayish-white, firm and adherent to the spinal cord and meninges. Frequently they invade the parenchyma of the spinal cord itself. The spinal cord may be compressed or present an irregularly swollen appearance, while the adjacent leptomeninges may be thickened and opaque.

A second less common form of metastasis is diffuse meningeal involvement. The pia mater is discolored and opaque and the leptomeninges may be covered by a layer

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of tumor tissue varying in thickness from a thin film of tumor cells to a sheet of neoplastic tissue several millimeters in thickness.

On microscopic examination such spinal tumors are usually similar in appearance to the parent intracranial neoplasm, especially the metastases which invade the spinal cord. However, those which invade the meninges, according to Wolf,[15] often present a somewhat different microscopic picture because of fibrosis in the neoplasm, which may give it a sarcomatous appearance.

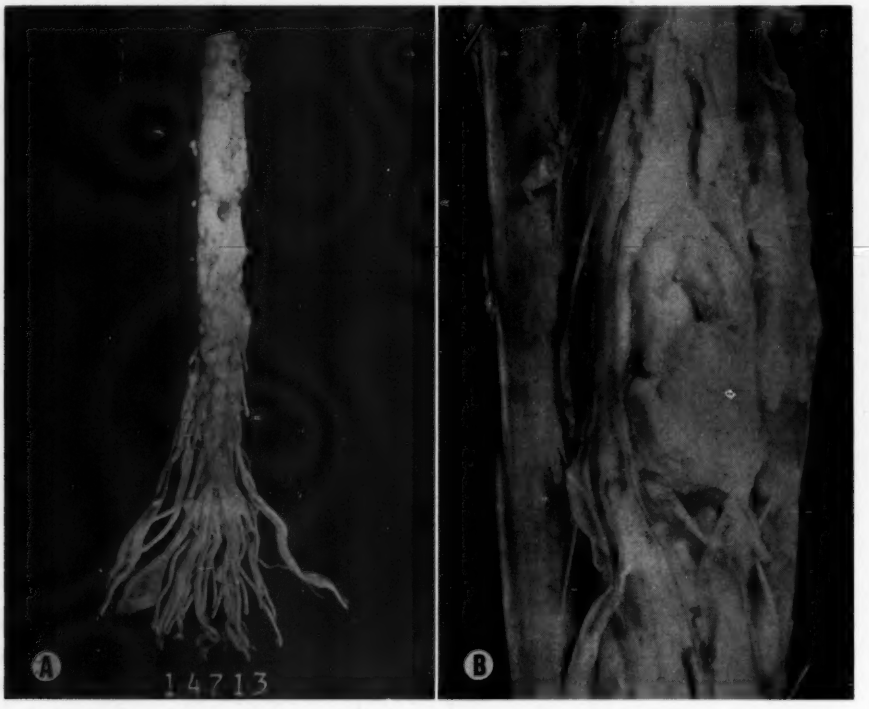

FIG. 1. Metastatic glioblastoma multiforme of the spinal cord and cauda equina from the left frontal lobe of the brain. Numerous nodules are visible en face on the dorsal aspect of the spinal cord and in profile on the lateral surface (*A*). The spinal cord appears larger than usual and the surfaces are irregular. A number of small metastatic masses are attached to roots of the cauda equina.

Low power magnification of one of the spinal cord lesions (*B*) reveals an oval tumor attached to the spinal cord. The normal external configuration of the spinal cord is destroyed. The pia mater is thickened and at many points is not transparent. The pia is not visible over the metastasis which is primarily subarachnoid in location but invades the spinal cord through its inner membrane.

CLINICAL AND ROENTGENOLOGIC INVESTIGATION

It is a fairly common occurrence for patients with a cerebellar medulloblastoma or fourth ventricle ependymoma to develop symptoms and neurologic signs suggesting spinal cord metastases from a few weeks to several years after the primary tumor is discovered. Symptoms may vary from back pain and radicular pain to a syndrome of spinal cord compression with weakness and numbness of the lower extremities, and if the cauda equina is involved, sphincteric disturbances may be prominent. Larger metastases which compress or invade the spinal cord may of course produce a spastic paraplegia with a well defined sensory level.

Examination of the cerebrospinal fluid in such cases generally discloses pleocytosis, an increase in protein content and a partial or complete obstruction of cerebrospinal fluid. Cytological study of a centrifuged

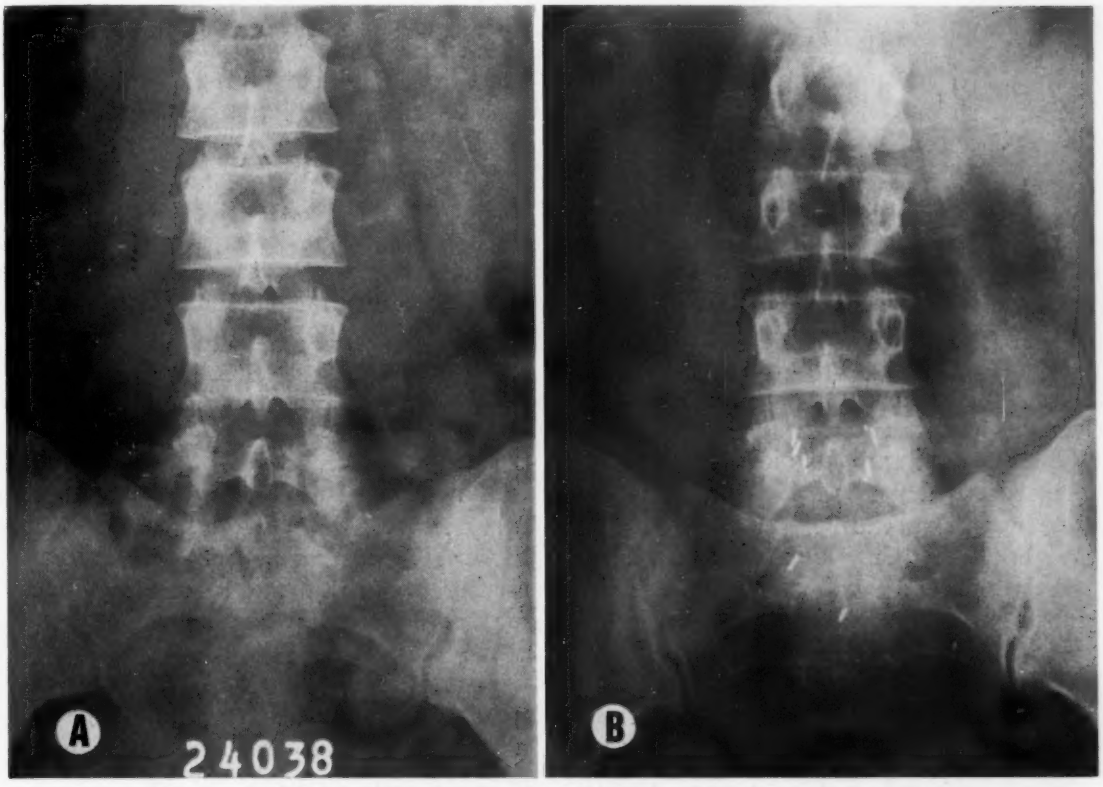

Fig. 2. Silver clips in lumbosacral subarachnoid space following intracranial surgery. A twenty-eight year old woman had a suboccipital craniectomy with subtotal removal of a hemangioblastoma of the cerebellum in 1932. A survey film of the abdomen (*A*) was made in 1936, in which the lumbosacral portion of the spine can be seen clearly, and no silver clips are present in the lower subarachnoid space at this time, which indicates that the clips were not misplaced at the time of intracranial surgery.

The patient was readmitted in 1941 because of pain in the low back and in both lower extremities. A plain film of the vertebral column (*B*) made at this time discloses a number of silver clips in the lower vertebral canal at the level of L-5, S-1 and S-2. At operation a hemangioblastoma which filled the mid and lower lumbar portion of the subarachnoid space was disclosed. The possibility of neoplastic cells being carried to the lower subarachnoid space by silver clips during their descent is suggested.

sediment from the cerebrospinal fluid may reveal the presence of neoplastic cells in the fluid. Indeed, Merriam[9] has recently described the detection of neoplastic cells in the cerebrospinal fluid of a patient with intracranial extension of retinoblastoma.

Ordinarily, no abnormalities resulting from neoplastic metastasis are disclosed in plain roentgenograms of the spine. However, the gravitation of hemostatic metallic clips used in intracranial surgery at the time a primary neoplasm is evacuated has been observed from time to time (Fig. 2), and the possibility of silver clips carrying neoplastic tissue from the brain to the spinal cord has been mentioned by Halpern.[5] While the injection of lipiodol to localize a metastatic ependymoma compressing the spinal cord was carried out preoperatively on one occasion by Tarlov and Davidoff,[13] the use of myelography to determine the presence, extent and exact location of metastatic masses for radiation or surgical therapy has not been given much attention.

MATERIAL

During recent months myelography has been found useful in the evaluation of suspected spinal cord metastasis from primary brain tumors in 4 patients, 2 with cerebral glioblastoma multiforme (Fig. 3) and 2 with cerebellar tumors histopatho-

logically identified respectively as medulloblastoma (Fig. 4) and hemangioblastoma (Fig. 5). In 3 of these cases the metastases primarily involved the spinal cord. In the fourth case lesions were demonstrated only in the cauda equina.

In all 4 cases myelography disclosed multiple filling defects in the contrast outline of the subarachnoid space. The defects appeared as rounded or oval areas of diminished density in the pantopaque column which varied in size from less than 1 mm. to 2 cm. in diameter. It was possible to establish the presence of these lesions by reproducing the filling defects in the myelogram with repeated passage of pantopaque into the involved areas. In one instance a thoracic spinal cord implant was sufficiently large to cause a partial obstruction to the flow of pantopaque while in another patient large masses in the lumbosacral culde-sac caused complete obstruction to the caudad flow of opaque oil. The fact that the spinal cord was usually not displaced from its normal position, as ordinarily occurs with extramedullary tumors, may be explained by the presence of multiple masses on all sides of the spinal cord which prevented a gross shift in any one direction.

The opportunity of performing myelography before and after irradiation of the spinal cord metastases was afforded in 2 instances (Case I and Case IV). In the first patient, disappearance of some of the filling defects in the cervical and thoracic subarachnoid space and reduction in size of other defects, associated with neurological improvement, clearly indicated the efficacy of roentgen treatment in shrinking the glioblastoma multiforme metastases in this case. In the second patient metastatic nodules from a cerebellar hemangioblastoma were reduced slightly in size by spinal irradiation.

COMMENT

It is evident that a variety of primary cerebral and cerebellar tumors, and even tumors of the eye, may frequently metastasize to the spinal cord by way of the cerebrospinal fluid circulation. The diagnosis of such metastases is justified when symptoms of radicular pain or signs of progressive weakness not attributable to the intracranial tumor become established. Yet the presence of such lesions cannot always be determined by clinical examination, and their multiplicity may preclude accurate localization. Moreover, examination of the cerebrospinal fluid is usually not of great diagnostic value unless a complete obstruction is present or free tumor cells are found in the fluid. Finally, plain roentgenograms of the spine disclose no abnormality unless descent of silver clips from the primary tumor area to the vertebral canal suggests the possibility of metastasis. Myelography, therefore, becomes a useful means of detecting and localizing metastatic masses for treatment by irradiation and/or decompressive surgery.

Differential diagnosis of spinal cord metastases from other multiple tumors of the spinal cord is usually not difficult by myelography, especially as the presence of metastasis may be suspected after intracranial surgery. However, it is necessary at myelography to consider multicentric gliomas of the spinal cord, spinal cord tumors extending into the subarachnoid space, multiple neurinomas, meningeal tumors, dermoid cysts and lipomas, as described by Lichtenstein,[7] Camp[2,3] and O'Connell.[10] Intramedullary tumors, whether of single or multiple points of origin, tend to expand the spinal cord so as to produce at one or more levels in the myelogram a fusiform widening of the cord shadow. Extramedullary intradural tumors, on the other hand, displace the spinal cord sharply while the well delineated margins of the encapsulated tumor do not fuse with the shadow of the cord in the myelogram.

Since metastatic lesions are more common on the dorsal aspect of the spinal cord than elsewhere, and since this portion of the subarachnoid space is not generally visualized as well by myelography as the ventral and lateral portions of the canal,

the use of more than the average quantity of contrast material (9 to 12 cc. instead of 3 to 6 cc. of pantopaque), or rotation of the patient to the supine position, should be used in such cases to facilitate examination of the dorsal aspect of the spinal cord, especially in the thoracic area.

The metastatic nature of spinal hemangioblastoma occurring concomitantly with cerebellar hemangioblastoma may be open to question. While Wyburn-Mason[16] and other authors who have studied Lindau's[8] disease assert that the lesions are multicentric rather than metastatic, the presence of hemangioblastoma at the cerebellar surface or the fact that surgical evacuation has been done both suggest the possibility of its spread to the subarachnoid space. The majority of primary spinal hemangioblastomas studied by Turner and Kernohan[14] and by Wyburn-Mason[16] were solitary and intimately associated with the spinal cord itself. However, the multiple tumor nodules in Case IV were located in the lumbosacral portion of the subarachnoid space below the level of the spinal cord. It is also of interest to note that the spinal hemangioblastoma presumed to have been carried by metallic clips into the vertebral canal (Fig. 2), was located primarily cephalad to the clips. In this case the relationship of the silver clips to the metastatic nodules strongly suggests that the descent of the clips antedated the obstruction of the subarachnoid space by tumor.

Turning now to the effect of roentgen therapy upon spinal metastases as observed in serial myelograms, it has been observed in one instance of metastatic glioblastoma multiforme that spinal irradiation caused prompt shrinkage of multiple subarachnoid tumor masses. While the patient's subsequent course indicated that the regression of tumor was temporary, radicular pain was relieved and leg and bladder function were improved for several weeks after roentgen therapy. In another patient with hemangioblastoma, myelography demonstrated appreciable reduction in size of the neoplastic masses after spinal irradiation although shrinkage was less dramatic than in the case of glioblastoma multiforme.

In view of the controversy as to whether roentgen therapy is effective for cases with cerebral glioblastoma multiforme, the observations on Case 1 seem particularly significant. For this in essence represented a pure transplant of glioblastoma multiforme in the spinal subarachnoid space which was clearly reduced in size by roentgen therapy.

REPORT OF CASES

Case 1 (Fig. 3). A fifty year old woman (Unit No. 972673) was admitted to the hospital because of headache, nausea and occasional vomiting for five months. During the same period she experienced dizziness, faintness and a ringing noise in both ears. Loss of consciousness occurred on two occasions during the month before entrance to the hospital.

The patient had an unsteady gait, a positive Romberg test, and a tendency to fall towards the left with the eyes closed. A slight right facial weakness, nystagmus on right lateral gaze and bilateral papilledema of 3 diopters were observed.

Occipitoparietal ventriculography disclosed a multicystic tumor of the right frontal lobe in communication with the anterior horn of the right lateral ventricle. It is noteworthy that the ventricular fluid was slightly turbid and that neoplastic cells were identified on microscopic examination of a smear of the fluid.

A radical right frontal lobectomy was performed with evacuation of all possible tumor. The right lateral ventricle was opened widely during the operative procedure and direct communication of the tumor with the ventricle, as indicated by ventriculography, was verified. Microscopic examination of specimen of the tumor by Dr. Abner Wolf disclosed an astrocytoma undergoing glioblastomatous transformation.

Following operation radiotherapy was given to each lateral area until an estimated tumor dose of 2,000 r had been delivered in twenty-five days. A second course of irradiation was given two months later, an estimated tumor dose of 1,500 r being administered in eighteen days. The patient failed to return for a third course of irradiation which had been planned at the outset.

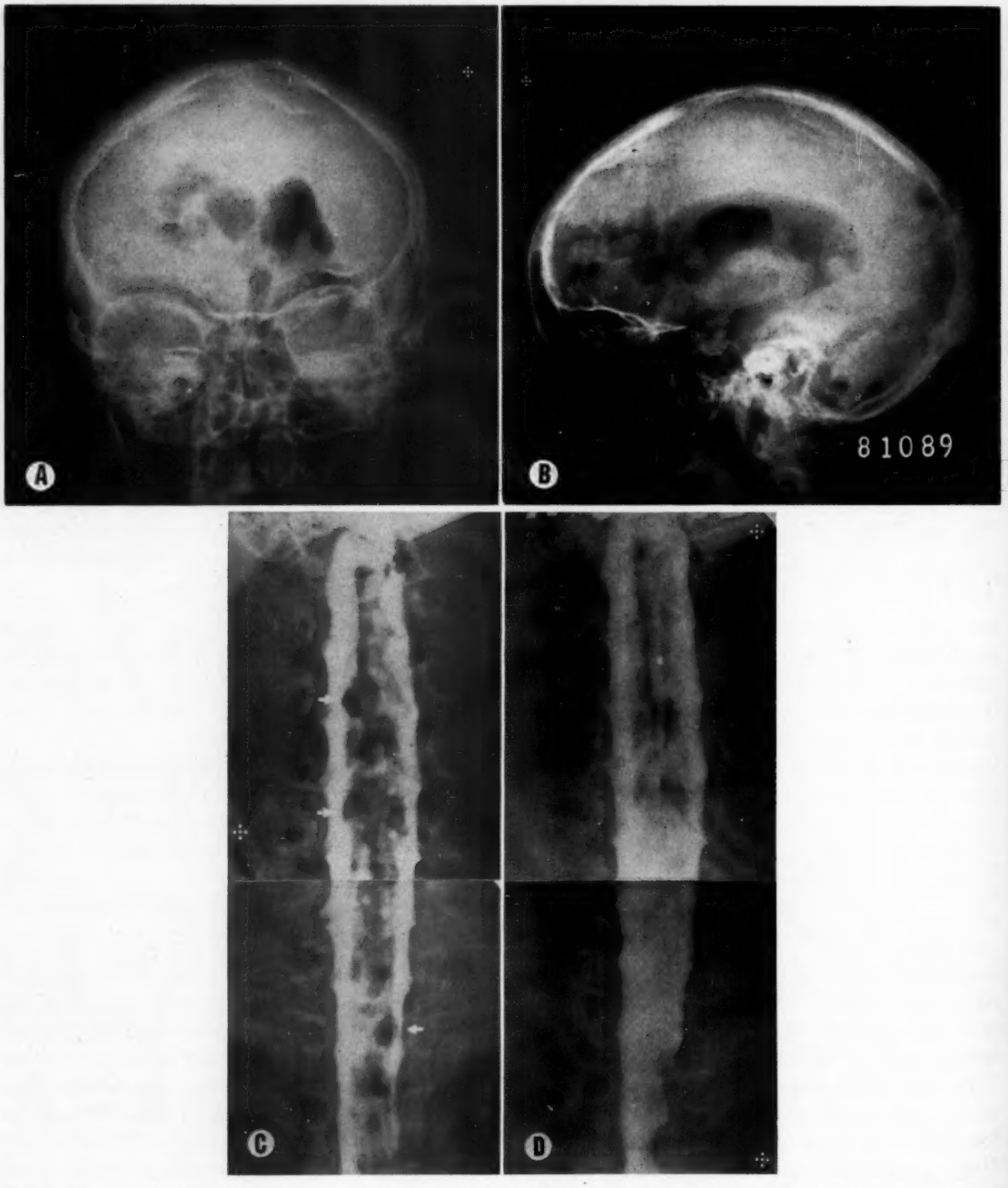

FIG. 3. Case 1. Cystic glioblastoma multiforme of the right frontal lobe with metastases to the cervical and upper thoracic spinal cord (before and after irradiation). Ventriculograms, in frontal (*A*) and lateral (*B*) projections, made with the patient supine, disclose a tumor of the right frontal lobe with compartments which contain fluid and gas as a result of communication with the anterior horn of the right lateral ventricle. Microscopic examination of a smear of the ventricular fluid at the time of this examination revealed tumor cells.

Myelograms (*C*) made nine months after incomplete removal of the intracranial tumor, disclose multiple, well defined, rounded filling defects in the pantopaque outline of the subarachnoid space resulting from implantation of metastases upon the spinal cord (arrows). Myelography (*D*) performed nineteen days later reveals that the metastatic masses disappeared following the administration of 1,000 r in air through fields directed toward the posterior aspect of the cervical and upper thoracic spine.

Nine months after operation the patient was readmitted to the hospital because of pain in both arms and in the right lower extremity of four weeks' duration. During the interval of eight months prior to the onset of these symptoms, there had been no advancement in neurological deficits and no new symptoms referable to the cerebral tumor had appeared. During the four weeks' period preceding the second admission both legs had become progressively weaker until the patient was unable to walk. Shortly before admission, frequency and urgency of urination developed and there was pain in the lower back.

On neurological examination the patient had a spastic paraparesis with such weakness that she was unable to stand. Generalized weakness in the arms was present also, but this was not as marked as in the legs. Deep tendon reflexes were slightly hyperactive in both upper extremities but reduced in the lower extremities, while bilateral positive Babinski reflexes were elicited. A suggestive level of impaired sensation for pain was demonstrated at the sixth thoracic dermatome. There was no papilledema nor cranial nerve signs.

Myelography with pantopaque disclosed numerous rounded filling defects in the contrast outline of the subarachnoid space which were most numerous in the cervical area (Fig. 3), where a mass measuring 1 cm. in diameter was present on the ventrolateral aspect of the spinal cord at C-4. The majority of the filling defects were readily reproduced on repeated passage of the opaque oil through the various parts of the canal. Delay in passage of the opaque oil was encountered at T-8 where a rounded filling defect continuous with the spinal cord shadow was visible at roentgenoscopy and demonstrated on the films.

Radiotherapy was administered to the entire spine through three fields. The patient began to regain strength in the upper and lower extremities shortly after the beginning of irradiation, and before 1,000 r had been given in air to each of the three fields the pain had disappeared. Another myelogram, made nineteen days after the first one, showed that most of the filling defects in the pantopaque column were no longer present. The few which remained could be constantly reproduced but were smaller than on the first myelographic examination. Following this, further irradiation was given until an estimated 1,500 r had been delivered to the metastatic lesions. At this time the patient was discharged from the hospital free of pain, and able to walk with minimal assistance.

Case II. A forty-six year old woman (Unit No. 976872) entered the hospital because of headache for six months. For one year the patient had experienced episodes of dizziness and for nine months had occasionally noted foul odors. A speech disturbance had been present for five months and for several days the patient had complained of double vision.

Neurological examination revealed a right hemiparesis with more weakness in the arm than in the leg. Posture-holding was performed poorly with the right arm and dysmetria was also present. Early papilledema and a moderate degree of aphasia were also observed. The clinical diagnosis of a left temporal lobe tumor was substantiated by electroencephalography.

At operation a large soft tumor was found, infiltrating the greater portion of the left temporal lobe. As much tumor as possible was evacuated, approximately four-fifths of the temporal lobe being removed. The final microscopic diagnosis was glioblastoma multiforme.

The patient's condition was satisfactory for nine months following operation, at which time she again developed difficulty in speech and olfactory hallucinations. At this time a new symptom of pain in the back of the neck and lumbosacral region developed. The patient was readmitted to the hospital where a myelogram disclosed multiple constant filling defects in the contrast outline of the subarachnoid space. The largest of these defects was located at the level of L-4 in the dorsal portion of the subarachnoid space and appeared as a bilobular area of diminished density which measured 2 cm. in its greatest diameter. Numerous other smaller defects were demonstrated in the mid and lower portion of the cervical canal. These were interpreted as representing metastatic masses implanted upon the spinal cord and cauda equina from the cerebral glioma.

Case III (Fig. 4). A fifteen year old boy (Unit No. 837534) entered the hospital because of headache and blurred vision for three months. During the same period he became fatigued easily and frequently complained of being drowsy. For one month before entering the hospital there was increase in dizziness, a tendency to fall towards the right, and frequent vomiting.

The patient walked with a broad gait and

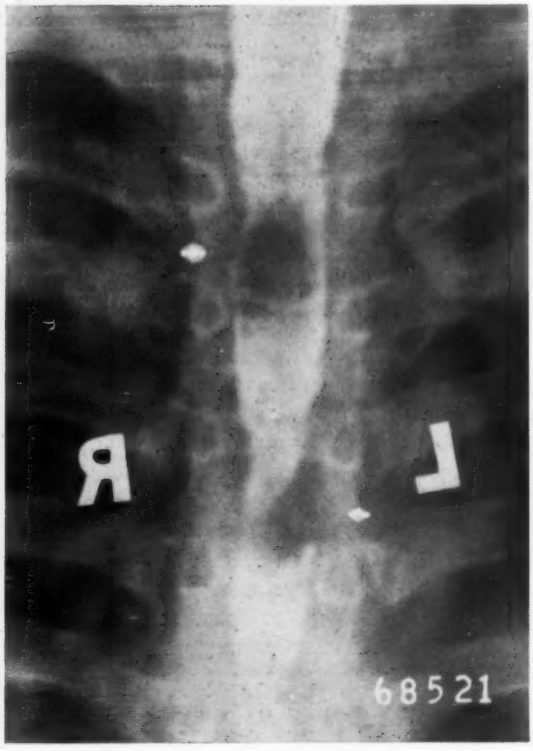

FIG. 4. Case III. Medulloblastoma metastases from the cerebellum to the thoracic spinal cord. Well defined oval filling defects in the pantopaque outline of the thoracic subarachnoid space are shown at the level of T-3 and T-5 (arrows). The outline of the upper mass is continuous with that of the thoracic spinal cord. The inferior lesion is attached both to the spinal cord and to the meninges but the spinal cord does not appear displaced by the lesion.

consistently veered toward the left. Non-equilibratory coordination was impaired in both upper and both lower extremities. Papilledema with 4 diopters' elevation of the optic disc was observed bilaterally.

At operation a large tumor of the cerebellar vermis was found extending into and filling the fourth ventricle. As much of the tumor as technically possible was excised but some of it was left along the floor of the fourth ventricle at its attachment to the brain stem. The microscopic diagnosis was medulloblastoma.

The patient received extensive radiation therapy administered to each side of the posterior fossa and over the entire spine while he was in the hospital and following his discharge, with marked improvement in his general condition and neurological status. His condition remained satisfactory for two years, but at the end of this time he was readmitted to the hospital because of numbness and weakness of the legs of three weeks' duration, which progressed rapidly until the patient was unable to walk. Pain in the thoracic and lumbar spine was also present during this period and loss of bladder control was present by the time of admission. The patient had a spastic paraplegia with a level of impaired sensation in the mid-thoracic region.

This patient was the first of a group to have a myelogram, which was performed because the patient previously had extensive irradiation to the spine and it was considered desirable to localize the spinal lesion, presumably metastatic, as accurately as possible before either surgery or further irradiation was carried out. The cerebrospinal fluid removed at the time of myelography contained 3,500 mg. protein per 100 cc. Roentgenoscopy disclosed a partial obstruction to the flow of pantopaque in the subarachnoid space at T-5/6, where an oval shadow of diminished density was present continuous with the outline of the thoracic spinal cord (Fig. 4). Similar reproducible filling defects in the subarachnoid pantopaque column were demonstrated on the films at T-3/4 and at T-12. These large metastatic masses were effectively treated with radiation therapy without recourse to surgery.

CASE IV (Fig. 5). A sixty year old man (Unit No. 901867) complained of periodic headache for two years before admission to the hospital. For six months frequent cramps occurred in the hands and thighs and the gait became unsteady. Frequent vomiting, double vision and buzzing noises in the left ear were experienced for four months.

The patient walked with a broad unsteady gait and dragged the right foot. Coordinated movements were impaired in both lower extremities. Paresis of the right sixth cranial nerve was present and bilateral papilledema with hemorrhagic exudates was observed on fundoscopic examination.

At operation a right cerebellar tumor was encountered which extended to the surface of the cerebellum and the right cerebellopontine angle. The tumor was extremely vascular and complete removal was impossible because of profuse bleeding. The microscopic diagnosis was hemangioblastoma.

Following operation the patient received three courses of roentgen treatment through fields directed toward each side of the posterior fossa. The courses of treatment were given approximately two months apart. Six months

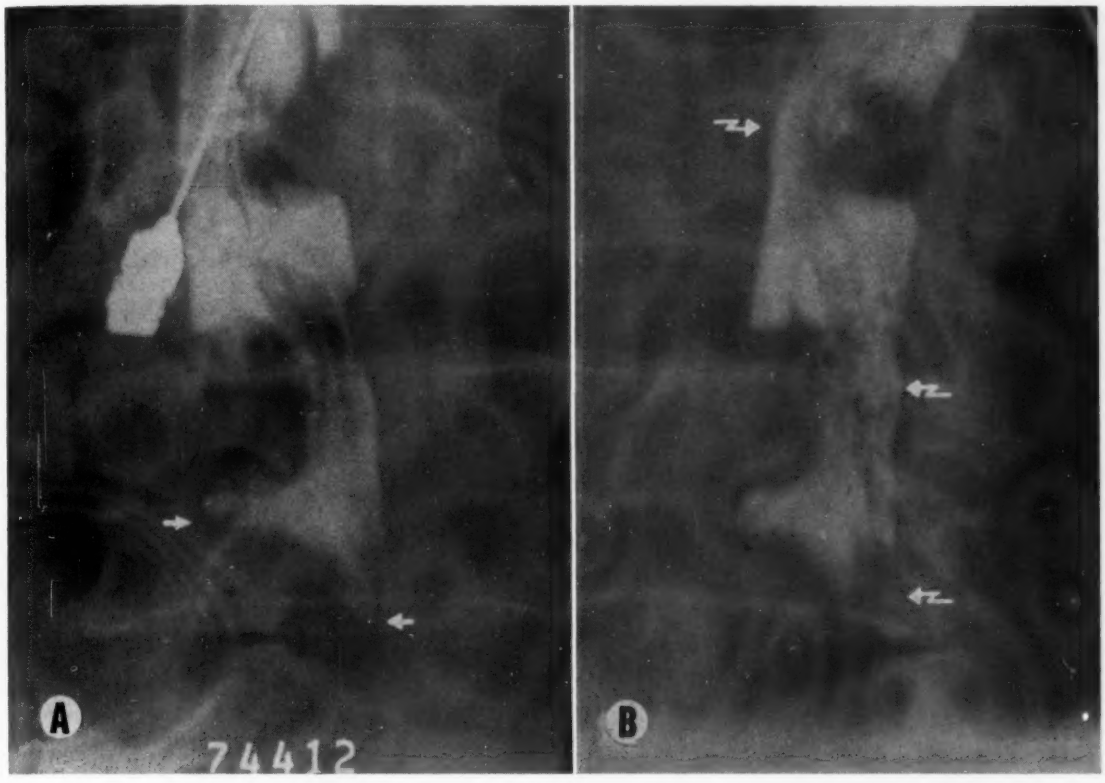

Fig. 5. Case IV. Multiple tumors of the cauda equina, presumably metastatic hemangioblastoma from the cerebellum. Complete obstruction to the caudad passage of pantopaque is demonstrated at L-4 in a frontal film (*A*) made with the patient standing. The margin of a smooth intradural tumor is outlined by the inferior portion of the pantopqaue column (straight arrows). Two non-obstructing masses are demonstrated more cephalad at L-4 and at L-3. The oblique projection (*B*) demonstrates to best advantage displacement and distortion of the cauda equina roots (wavy arrows) opposite the tumors.

after operation an estimated tumor dose of 3,200 r had been delivered to the cerebellar region. Subsequently the patient complained only of slight unsteadiness in gait and resumed full activity as a construction foreman.

The patient was readmitted to the hospital two years following operation because of increased unsteadiness of gait, nausea, vomiting and blurred vision. A second operation was performed consisting of a suboccipital decompression and partial evacuation of the right cerebellar tumor. Postoperative irradiation was again given to the cerebellar area with an estimated tumor dose of 1,500 r being delivered in a period of two weeks.

A third admission was necessitated six months after the second operation because of severe rectal pain. Questioning disclosed that this pain had been present, especially when the bowels moved, for approximately one year, and had been attributed to hemorrhoids. For two months before the third admission the rectal pain had become constant and increasingly severe until the patient was unable to sleep at night. The patient again exhibited moderate unsteadiness of gait and coordinated movements were performed poorly on both sides. Only mild weakness of the lower extremities was present and no sensory disturbances were elicited.

A myelogram performed at L-2/3 disclosed an obstruction to the caudad flow of pantopaque at the level of the inferior margin of L-4 (Fig. 5). With the patient upright, the lower end of the pantopaque column was concave, which was interpreted as indentation of the column by the superior surface of a large tumor filling the lower portion of the subarachnoid space. Just above the level of the obstruction, two other large filling defects in the contrast outline of the subarachnoid space were consistently demonstrated, one at the level of the upper margin of L-4 and the other at the level of the upper margin of L-3, each mass measuring approximately

2 cm. in diameter. Similar smaller defects were encountered at T-12 and at T-10, but above this area no abnormalities were demonstrated. The lesions were interpreted as representing multiple metastatic masses of hemangioblastoma of the spinal cord from the cerebellar tumor.

The effect of radiation therapy to the metastatic lesions could be observed because part of the pantopaque was left in the subarachnoid space. An estimated tumor dose of 2,500 r was delivered to the lesions through right and left lateral, and posterior portals over the lumbosacral spine. Roentgenoscopy was performed and films made at various intervals throughout the course of radiation therapy. At the end of the course of treatment the pantopaque obstruction had been relieved and the opaque material could be passed into the sacral cul-de-sac. Although shrinkage of the cauda equina masses was observed, the lesions failed to disappear entirely. The surgical excision of the residual tumor was not considered necessary at this time.

SUMMARY

1. Spinal cord gliomatosis may result from the spread of a variety of primary cerebral and cerebellar tumors by way of the cerebrospinal fluid circulation.

2. Myelography is a satisfactory method of detecting and localizing such spinal metastases when clinical diagnosis is uncertain.

3. Spinal metastases of this type characteristically produce multiple well defined, anisometric, smooth, rounded filling defects in the contrast outline of the subarachnoid space, and when large, may produce an obstruction to the passage of opaque material.

4. Myelography is an aid in the direction of radiation and surgical therapy, and may be useful to evaluate the results of treatment.

5. In one case (Case 1) myelography clearly showed the beneficial effects of roentgen therapy on a pure transplant of glioblastoma multiforme in the spinal subarachnoid space.

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THE VALUE OF PANTOPAQUE MYELOGRAPHY IN THE DIAGNOSIS OF HERNIATION OF THE NUCLEUS PULPOSUS IN THE LUMBOSACRAL SPINE

A REPORT OF 500 CASES*

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MYELOGRAPHY has been used extensively as a diagnostic procedure since it was first introduced. Many articles have been published on all phases of the subject and new reports are constantly being added. The following is a report of 500 pantopaque (lumbar) myelograms done at Hines Hospital between May, 1946, and May, 1950, with an analysis of the myelographic, clinical and surgical findings in 414 cases.

All the patients were thoroughly studied on the Neurosurgical Service and routine anteroposterior and lateral films of the lumbosacral spine were made before myelography. None of these patients were operated on without prior myelography. As the technique of myelography has been adequately described in the literature, only a brief outline of our current method will be given. The lumbar puncture is done with the patient either prone or lying on his side. The contents of one ampoule of pantopaque, 3.0 to 3.4 cc., is introduced into the spinal canal and the needle is then withdrawn. The canal is then examined roentgenoscopically from the cul-de-sac to the first lumbar interspace. (As an added precaution, the patient's head is hyperextended at all times while the foot of the table is elevated.) Spot roentgenograms are made as indicated in the prone anteroposterior and oblique positions (and at times, lateral, with the overhead tube). The films are inspected wet with the oil still in the canal to permit additional views as required. The needle is then reinserted at the lowest practicable level and the pantopaque removed by aspiration; however, occasionally straining is required to accomplish removal. A final anteroposterior spot roentgenogram of the lumbosacral region is then taken.

First, a brief discussion of the findings on routine roentgenograms of the lumbosacral region will be given. The increased frequency of narrowing of the lumbosacral space associated with backache has been recorded by various observers. For example, Hodges and Peck found a narrow lumbosacral space in 57.2 per cent of 446 cases of low back pain with sciatic radiation, but in only 12.8 per cent of 538 cases without such radiation; they do not, however, given the incidence of herniated disc in these groups. The following facts are known concerning the relation of narrowing of the intervertebral spaces to herniation of the disc:

1. Narrowing of the interspace may occur in the presence of herniated disc.

2. Herniation of the disc frequently occurs without narrowing of the interspace. Ferguson states that herniation of the lumbosacral disc occurs just as often with narrowing as without. In 100 case of herniation of the lumbosacral disc, we found a normal lumbosacral space in 45, definite narrowing in 30, and questionable narrowing in 25.

3. Narrowing may occur without any herniation of the disc. Peyton and Simmons reported several such cases. Willis points out that narrowing may be a mani-

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festation of partial sacralization and that the lumbosacral disc may vary from the thin sacral to the thick lumbosacral type. Ferguson, Ramsey, French and Strain, and others, note that narrowing may be a manifestation of the normal process of age, underdevelopment, degeneration or change in the surrounding bone.

4. Narrowing of the fourth lumbar disc is more significant. It was found in one-third of the herniations at that level by Hampton and Robinson.

5. When accompanied by sclerosis and local hypertrophic changes, narrowing is more significant but is by no means pathognomonic. We found occasional instances of narrowing and sclerosis at both the fourth and fifth lumbar discs without herniation. Camp noted hypertrophic changes in 17 cases out of 50 herniated discs, but in only 5 were the changes sharply localized to the site of the herniation.

In summation, it may be stated that roentgenographic changes are not specific in herniation of the nucleus pulposus when present and are frequently not present. However, the routine roentgenograms are of considerable importance from the standpoint of excluding other lesions such as tumors of the vertebrae, infections and anomalies as emphasized by Bradford and Spurling.

Of the 500 patients who had myelography, 414 were operated on: 66 of those with negative myelograms and 20 of those with myelographic defects were not subjected to surgery. The myelographic diagnosis was verified in 346 cases of herniated disc, 2 cord tumors and 8 negative cases—a total of 356, or approximately 86 per cent correct.

The myelographic diagnosis was in error in 58 cases, or 14 per cent. These errors consisted of the following:

8 negative myelograms in which herniated discs were found.
18 with myelographic defects in which no herniated discs were found, including 4 with two myelographic defects.
9 with two myelographic defects in which a herniated disc was present at one level but not at the other.
9 with two myelographic defects in which a herniated disc was present at one level but no exploration of the other level was done.
4 with myelographic defect at one level and herniated disc at a different level.
6 with myelographic defect in error as to the side of the lesion.
4 with equivocal myelograms—in 2 of these, herniated discs were found at surgery; in 1 of these, no herniated disc was found; and in 1, a herniated disc was found at one level but not at the other level suspected.

Further analysis of the myelographic defects reveals the following:

6 of the false negatives had herniated discs at L-5, S-1. Of these 6, 1 had considerable narrowing of the lumbosacral joint with sclerosis and also a broad spinal canal; 3 had a broad canal and a high sac ending just below the upper border of S-1.
1 of the false negatives had a herniated disc at L-5, L-6.
1 of the false negatives had a herniated disc at L-4, L-5.

The surgical findings in the 27 false positives were as follows:

8 bony abnormalities, of which only 3 were shown on the roentgenogram.
5 varices.
6 miscellaneous.
8 nothing at all.

The bony abnormalities consisted chiefly of subluxation and anomalies (not seen on routine films). The neurosurgeon found subluxation of L-5 on L-4 in 1 case with apparently complete block at the L-4, L-5 interspace (although some oil trickled by when the patient was placed on his side) (Fig. 1); there was also a mild osteoarthritis of the lumbosacral joint (on the roentgenogram). However, apparent block has been reported with no subluxation or other abnormality by Hibbard.

There were 2 cases with good myelographic defects between L-4 and L-5, 1 with marked narrowing of the interspace, sclerosis and spurring, and the other with similar but less marked changes (Fig. 3). One case had narrowing of the lumbosacral interspace, sclerosis and lipping; the nucleus pulposus was fragmented but not herniated and the annulus fibrosus was intact; also, the ligament between L-5

and S-1 was broken and a piece of the spine of S-1 was torn off (Fig. 4).

In at least 5 of the group with varices or miscellaneous changes, the myelographic defects were adequately explained by the surgical findings which were:

(1) A large varix compressing a nerve root.
(2) Neuroma of the nerve root.
(3) A ropy mass just below the left fifth lumbar root attached to the lateral wall of the spinal canal—this was associated with a congenital absence of the right lamina and a defect in the left lamina of S-1. The histopathology of this mass is not known as it was not deemed advisable to remove it (Fig. 5).
(4) A thick fat pad producing an atypical defect (Fig. 6).
(5) Postoperative adhesions (Fig. 7).

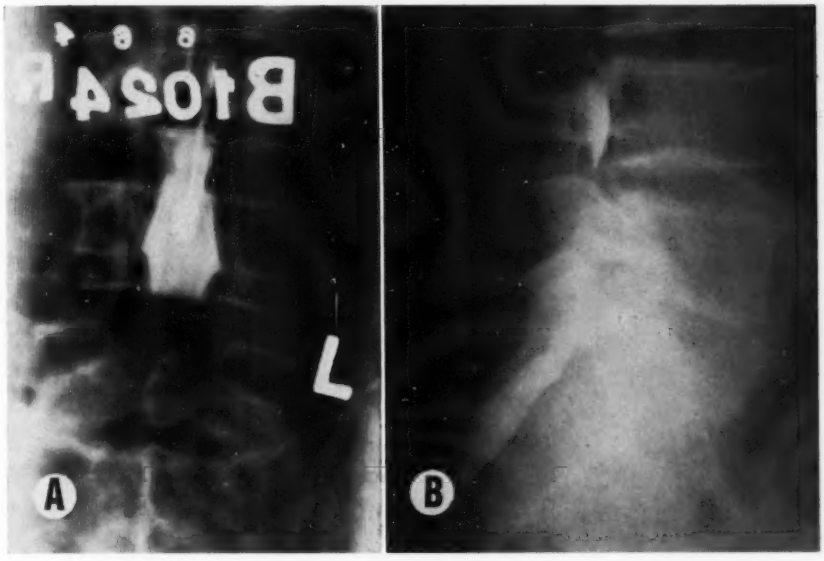

Fig. 1. (*A*) Apparently complete block at lower border of L-4. (*B*) Pantopaque largely passes through when patient lies on his side. No herniation but at surgery, subluxation of L-4 on L-5 was found.

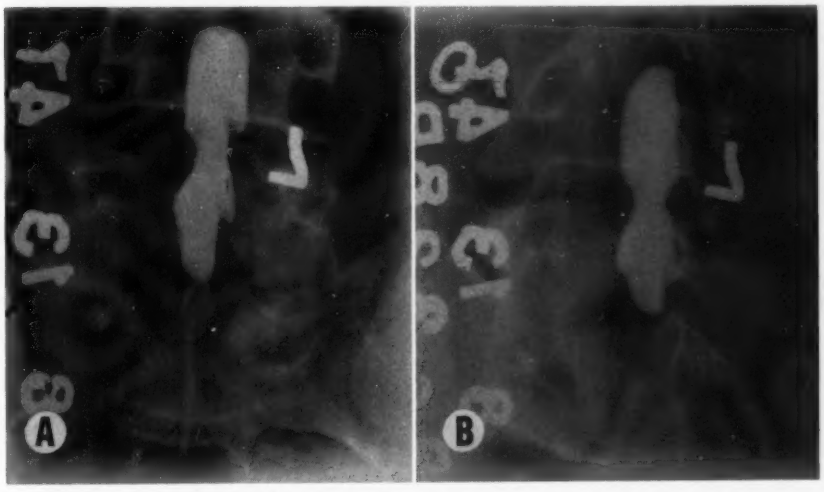

Fig. 2, (*A*) and (*B*). No herniation but subluxation of L-4 on L-5 was found at surgery.

Another defect was probably accounted for by a large group of epidural veins which almost constituted an angioma. In the remaining 2 cases of the miscellaneous group, a swollen nerve root was found in 1 and hypertrophic ligamentum flavum in the other.

Three of the 8 cases with no findings at

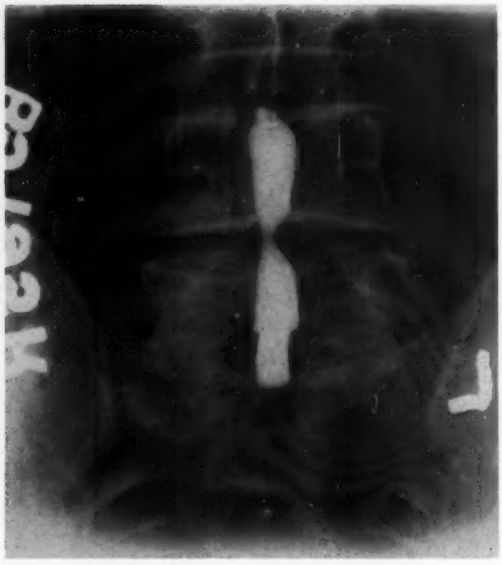

FIG. 3. Narrowing of L-4, L-5 interspace with marginal spurring. No herniation of the disc. At surgery, spinous process of L-5 impinged on lower border of L-4 and a large extradural vein was present.

surgery had sweeping right angle defects on the myelogram (Fig. 8); in 2 others, the pantopaque was markedly globulized.

Two of the 9 cases in which the second defect was not explored had symptoms on the side opposite the defect. A third had a right angle defect. It should be noted here that previous exploration of several other cases with right angle type of defect failed to reveal herniated discs, particularly at L-3, L-4; hence, our neurosurgeons hesitate to operate at this level in these cases, particularly if a lesion is found at a lower level.

The four errors in level of the herniation were as follows:

(1) Defect at L-5, L-6; lesion at L-6, S-1.
(2) Defect at L-4, L-5; lesion at L-5, S-1.
(3) Defect at L-5, L-6; lesion at L-4, L-5.
(4) Defect at L-5, S-1; lesion at L-4, L-5.

Of the 6 errors in localizing the side of the lesion, myelography placed 3 in the midline instead of laterally. In 1 of these, the ligamentum flavum was hypertrophied and there were postoperative adhesions. One was unilateral on the myelogram instead of midline; the other 2 were on the wrong side.

Considerable attention has been directed to the causes of myelographic error, particularly in the comprehensive article by Camp as well as the papers by Horwitz; Arbuckle, Shelden and Pudenz; Scoville, Moretz and Hankins; Maltby and Pendergrass; Ford and Key; and others. The errors culled from these reports may be divided into two main groups: (A) false negatives, and (B) false positives.

Group A consists of:

1. Protruded disc too far lateral to produce defect.
2. Unusually short cul-de-sac. (Horwitz found the cul-de-sac to end between S-1 and S-2 or at the body of S-2 in 54 out of 58 cadavers.)

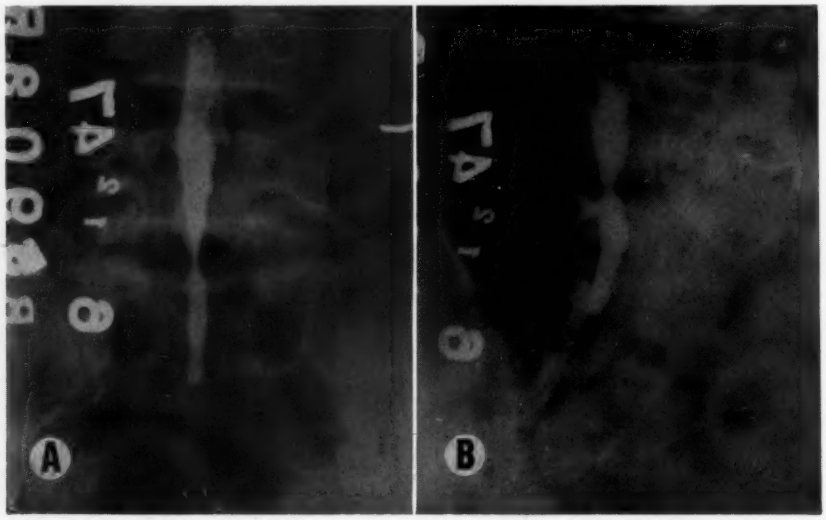

FIG. 4, (*A*) and (*B*). Nucleus pulposus fragmented but not herniated.

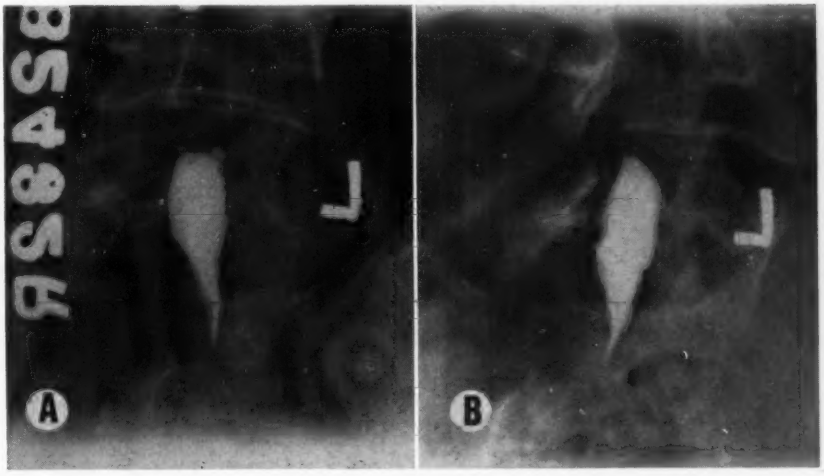

Fig. 5, (*A*) and (*B*). No herniation but mass found at right location to produce defect.

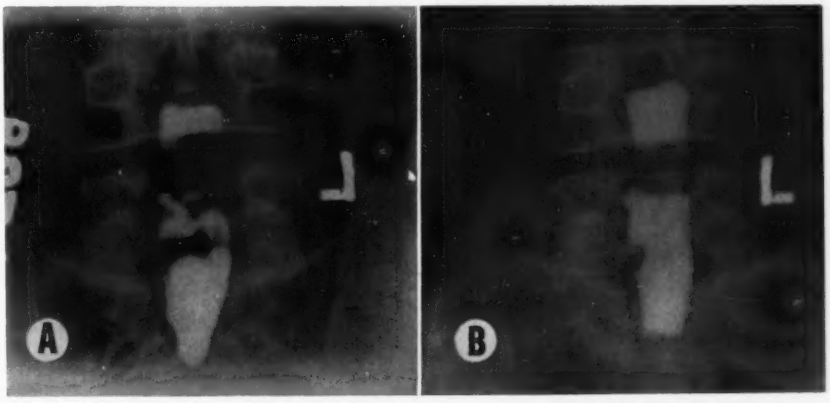

Fig. 6, (*A*) and (*B*). Irregular defect at L-5, S-1 due to thick fat pad. Note midline disc at L-4, L-5.

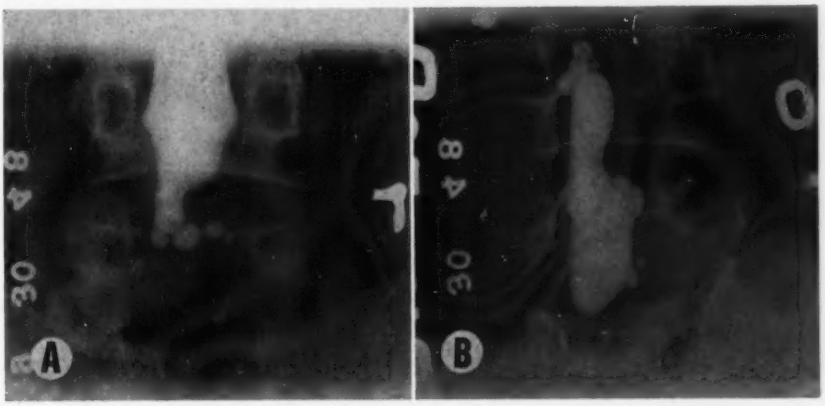

Fig. 7, (*A*) and (*B*). No herniation. Postoperative adhesions and large extradural veins.

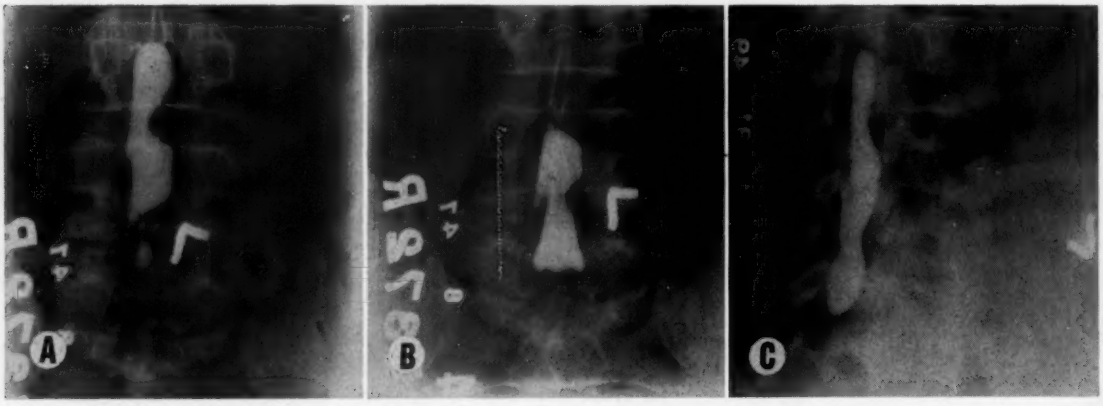

FIG. 8. (*A*) Nothing but large veins found at L-3, L-4. (*B*) Herniated disc at L-4, L-5. (*C*) Note anterior indentation at both L-3, L-4 and L-4, L-5.

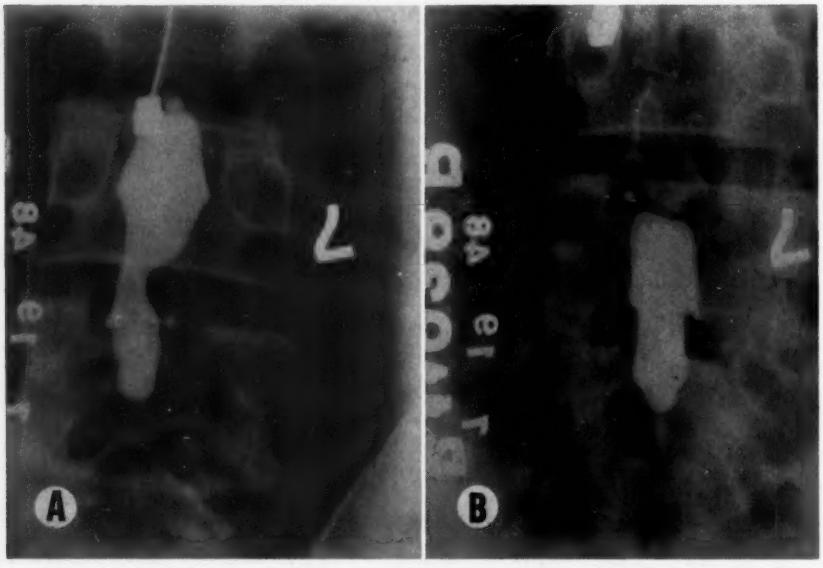

FIG. 9. (*A*) Sweeping defect but nothing found at L-4, L-5. (*B*) Herniated disc at L-5, S-1 on the right.

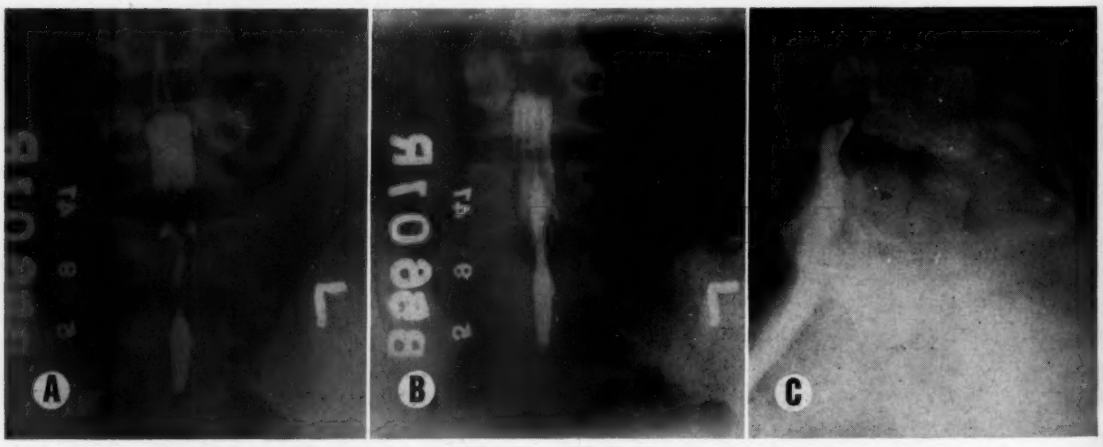

FIG. 10, (*A*), (*B*) and (*C*). Midline disc at L-4, L-5 with "veiled" defect demonstrated in (*B*). Second disc present at L-5, S-1.

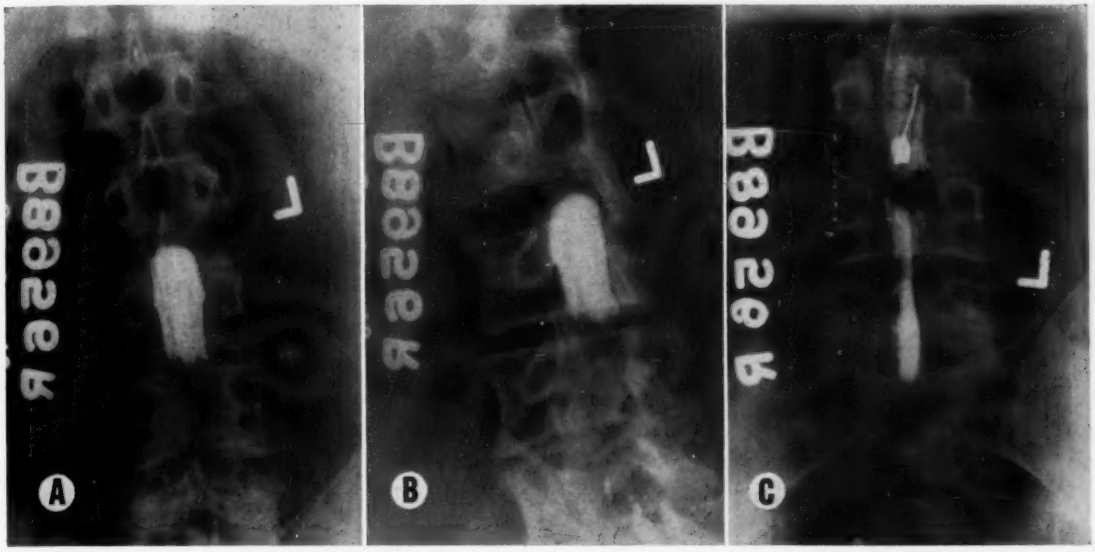

Fig. 11. (*A*), (*B*) Complete block at L-3, L-4. (*C*) One week later, pantopaque has descended to S-1. At surgery, subluxation of L-4 on L-3 and postoperative adhesion but no herniation.

3. Narrow canal, less than 16 mm.
4. Central herniation hidden by pantopaque ("veiled" defect) (Fig. 10).
5. Giant cul-de-sac.
6. Insufficient contrast material.
7. Concealed central disc (Dandy).
8. Multiple discs with single defect.

Group B consists of:

1. Bone changes including hypertrophy of the margins of the vertebral bodies and articular facets and degeneration of the disc.
2. Needle defects. These can be avoided by lumbar puncture above the usual sites of the lesions.
3. Varices.
4. Improper injection of the medium resulting in extra-arachnoidal oil and pseudo-defects.
5. Epidural abscess.
6. Hypertrophy of the ligamentum flavum.
7. Constriction at L-3, L-4 interspace due to stringing out of the oil.
8. Postoperative adhesions. These may result in smooth defects or even block, as well as the irregular defects.

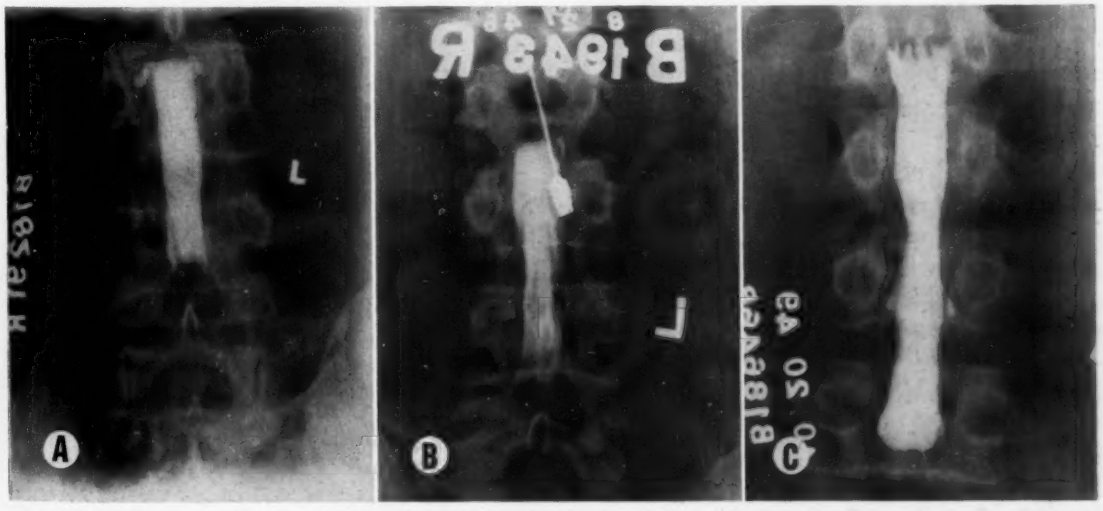

Fig. 12. (*A*) Complete block at middle of L-4 from high herniation of nuclear material. (*B*) Complete block at lower border of L-4 from extradural hemangioma. (*C*) Complete block at middle of L-1 from ependymoma of conus.

9. Defects from previous myelography or previous lumbar puncture.
10. Handicap due to patient's condition, deformities of the spinal column or inadequate apparatus.
11. Inadequate scope of examination.

Still another cause of errors is miscount of the anatomic level, particularly where anomalies of the fifth lumbar or first sacral segments exist.

Table 1 lists some of the statistics obtained from the literature and our own figures.

In the false negatives reported by Arbuckle, Shelden and Pudenz as well as in 10 cases in their series with questionable myelographic findings and herniated discs, the spinal canal measured 16 mm. or less in width.

As pointed out by Scoville, Moretz and Hankins, many statistical surveys give a high percentage of accuracy in myelography when only the positive myelograms are considered. On the other hand, if only the negative myelograms are analyzed, the percentage of myelographic errors is considerably higher. Although the total number of false negative cases which have come to our attention in a review of the literature has been rather small, it must be conceded that these constitute an important source of error. It is generally accepted that the most important causes of false negatives are laterally placed discs, narrow canal and short cul-de-sac. The greatest number of false negatives have been reported in herniation of the lumbosacral disc. The so-called concealed disc of Dandy is a moot point.

Thus far, the myelographic errors have been considered. The cases were next analyzed from the standpoint of the accuracy of the clinical diagnosis. Two hundred and ninety-six cases with definite clinical (and also myelographic) diagnosis of herniation of the nucleus pulposus were operated on.

In 167 of these, all the findings agreed; in 97 of these, the myelographic and surgical findings were in accord but the clinical level was in error; in the remaining 32 of these, the myelograms were in error—in 6 of these, the clinical and surgical findings agreed.

In 113 cases, herniation of the nucleus pulposus was suspected clinically but the level was not specified either because it was withheld pending myelography or because the findings were indeterminate. Ninety-eight of these were operated on. The myelographic findings were verified in 82 herniated discs and 2 cord tumors. In 1 cord tumor, where the block was at L-1

TABLE I

TABLE OF STATISTICS

Author	Total Number of Cases	Over-all Accuracy	Number of False Negatives	Over-all Per Cent of False Negatives	Total Negative Myelograms	False Negatives	Per Cent of Total Negatives
Camp	210	92.4%	7	3.45%	—	7	—
Arbuckle, Shelden and Pudenz	70	72.9%	7	10.0%	—	7	—
Maltby and Pendergrass	66	84.8%	4	6.0%	9	4	44.4%
Scoville, Moretz and Hankins*	196	67.0%	31	16.0%	—	31	—
Ford and Key	206	72.3%	27	13.0%	39	27	69.2%
Our series	414	86.4%	8	2.0%	16	8	50.0%

* Six cases were included with the false negative group in Scoville, Moretz and Hankins' series because only single defects were found myelographically but 2 herniated discs were present at operation.

myelographically, the clinical impression was a herniated disc in the lower lumbar region. In the remaining 14 cases, the myelogram was in error.

Of 16 cases with a clinical diagnosis of herniated disc but with negative myelograms, 8 were found to have herniated discs.

In the 4 remaining cases, the clinical diagnosis was correct in 2, wrong as to level in 1 and entirely wrong in the other, no disc being found. The myelographic findings in these were equivocal.

Thus, the clinical diagnosis was unqualifiedly correct in 183 out of 414 cases. While a disc was suspected in 98 others clinically, and verified surgically in 82, no level was specified in this group prior to myelography. If this last group is included with the clinically correct, the total correct would be 265, or 61.6 per cent, which is considerably less than the 86 per cent myelographically.

The foregoing is not intended to minimize the importance of the clinical findings, but merely to emphasize the difficulty of making an accurate diagnosis by clinical means alone. Many of the recent articles give considerable attention to myelographic errors but relatively little is said about the clinical accuracy.*

However, Dandy reported 63 consecutive cases without myelography in which the clinical diagnosis was verified. Bradford and Spurling state the correct clinical diagnosis was made in 80 per cent and that in 75 per cent or more of these, it is also possible to localize the lesion accurately by clinical findings. Keegan verified the location of the affected nerve root by means of dermatome hypalgesia in 588 cases of herniated discs of a total of 1,030 observed cases. He did not operate on the remaining cases. However, Keegan admits: (1) that a lesser degree of compression or intermittent compression of the nerve root may not give a definite dermatome pattern and hence the wrong disc can be explored; (2) a more lateral or more medial herniation may compress the nerve root below or above the usual root of the involved disc; and (3) two nerve roots may be compressed by wide herniation leading to more extensive hypalgesia and motor loss than usual. Keegan gives no statistics on how often these findings lead to error but says myelography may occasionally be indicated before operation.

The presence of multiple herniated discs constitutes a further reason for myelography. Camp noted an incidence of 18.8 per cent of such lesions; Ford and Key, 15.5 per cent; Scoville, Moretz and Hankins, 11 per cent, etc. In our own series, there were only 10 multiple discs, or just over 2 per cent, which is much lower than most published reports.

Myelography is of particular value in demonstrating tumors of the lower cord and the cauda equina. Toumey, Poppen and Hurley point out the great similarity of symptoms in cauda equina tumors and herniated discs and also the fact that tumors of the cauda equina at different levels may give approximately the same symptoms and signs. Toumey and his associates found 48 cauda equina tumors and 1,056 herniated discs, an incidence of 4.3 per cent tumors. Barr reports 15 tumors of the conus and cauda equina and 330 herniated discs, making approximately 4 per cent tumors. It is significant that several of Barr's patients with tumors had previous unsuccessful operations for herniated discs. In our series, there were only 2 tumors in 414 cases, or ½ of 1 per cent, a rather low figure compared to most reports. In addition, Camp stresses the importance of myelography in demonstrating multiple tumors or combinations of tumors and herniated discs. It is especially important that tumors may thus be localized before irreparable damage has been done and, hence, can be cured by surgery.

Because of the difficulties outlined above in the clinical diagnosis of herniated discs

* The authors do not mean to imply that they surveyed the entire literature on myelography, which has become quite voluminous. Thus, Bradford and Spurling, in 1945, listed 307 references while Pillmore, in 1947, gave 157 references (but included many of the first list).

and cord tumors, we are in accord with the group that believes myelography should be done in all these cases. However, all of the findings must be considered in evaluating each case and a negative myelogram should not be permitted to prevent exploration in the face of strong clinical findings. When the myelographic and the clinical findings are correlated, the best results are to be anticipated, and errors minimized.

There appears to be undue fear of pantopaque myelography by some authors. Dandy even wrote a fervent plea against its use. However, Barr states that no authenticated case of serious effects from its use occurred in over 500 examinations at the Massachusetts General Hospital. We have also had none in over 500 cases. Others have had similar experiences.

SUMMARY

1. Myelography should be done in every case where herniated nucleus pulposus is suspected, particularly where surgery is contemplated.

2. It is a procedure that is readily done in the average roentgen department equipped for spot roentgenography and is without serious effects.

3. Myelography is particularly valuable in accurately localizing herniated discs, demonstrating cord tumors when clinical findings are inadequate, and showing multiple discs and combinations of discs and tumors.

4. Myelography is not infallible and the various causes of errors have been considered.

5. A negative myelogram should be no deterrent to surgery in the face of strong clinical findings.

6. All of the findings must be considered in arriving at the final diagnosis.

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PHOTOFLUOROGRAPHY FOR THE DETECTION OF UNSUSPECTED GASTRIC NEOPLASMS*†

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INTRODUCTION

THIS paper will demonstrate that there is available a simple, accurate and practical photofluorographic method for the detection of silent gastric cancer and at least one of its precursors. The chief reason for considering this approach a practical one is that the ratio of physician-time consumption to ancillary help time consumption is minimal. It is approximately equivalent to that of chest photofluorography for tuberculosis. The need for the early diagnosis of gastric cancer is certainly as great as the need for early diagnosis in pulmonary tuberculosis. The death rates for the two diseases currently are about the same.

Any discussion of the essentiality of a medical procedure involves: (1) a summary of the pitiable conditions existing because of its lack; and (2) a refutation of the *suppositions* that the present situation is about the best attainable anyway. There seem to be about as many physician-philosophers writing why gastric surveys are impractical as there are physician-investigators trying to develop practical approaches.

The need is readily established. About 24,000 persons die of gastric cancer each year even now, because they reach the surgeon too late or are not diagnosed until dead.[3,9] Over one-fourth of the cancer deaths each year are due to gastric cancer;[54] recall that cancer ranks second as the cause of all deaths. In any four years as many people die of gastric cancer as there were United States soldiers killed in action during all of World War II. Of patients diagnosed as having cancer of the stomach, 62 per cent are dead in one year[10] and 93–98 per cent are dead in five years.[34,53] In over 20 per cent of autopsied cases with gastric cancer, the lesion is shown to have remained limited to the stomach and immediately adjacent nodes.[35] Only 14–25 per cent of the patients who reach the surgeon are suitable candidates for a curative type of operation;[13,54] and, finally, despite an increasing rate of operability and resectability and a decreasing surgical mortality rate, the total number of patients with arrested gastric cancer has not been significantly increasing.[18,45]

It is not possible to uncover every case of cancer of the stomach in this country; nor is it possible that every case found will be in an operable patient, nor that every resected case will live through the postoperative period. But it is possible to find most of the cases, and—considering some points even in their poorest light—it is possible to increase the operability rate if only by reducing the number that are now seen in terminal stages, and to increase the resectability rate by finding at least some of those cases that at autopsy do have limited disease. It is also possible, by finding smaller lesions, to reduce the surgical mortality rate, for there is a direct ratio between the size of the lesion and the surgical death rate.[53]

Excluding the grade of the neoplasm, over which we exercise no control, the primary factor affecting the surgical end results is the stage of general development, for when no apparent metastases are present, the five year survival rate is approximately 53 per cent and when metastases are present, it is but 18 per cent.[53]

It can be shown that we do have at least partial control over metastases. First, the

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discovery and surgical obliteration of a nonmetastasizing benign precursor of gastric carcinoma, the benign adenoma, precludes it from becoming a metastasis-producing lesion. Second, there is unequivocal evidence, despite contrary instances, that the smaller carcinomas have a lower rate of metastasis;[53] and the corollary to this is that earlier diagnosis (by definition) does result in smaller carcinomas and consequently a lower metastasis rate.

When consideration is given not only to the small and early neoplasms, but also to the large lesions, some of which have a slow growth potential and low metastasis rate, it is found that many remain undiscovered and symptomless for long periods, and then finally kill through size and resulting inanition, without producing distant metastases, always having been resectable.

And, finally, there is presented the following summary of what can be done, as accomplished by some who have been working with unsuspected as well as symptomatic cancer.

In 1934, Hauser[19,36] made the first known roentgenologic attempt to identify gastric cancer in asymptomatic persons aged forty and over. He found one examinee with carcinoma in the small group of 100 persons whom he examined. This case was operable and the lesion was resectable; there were no metastases. He is living today.

In 1944, St. John, Swenson and Harvey[49] reported on the results of a rapid roentgenoscopic survey of 2,413 persons, aged fifty or over, with no digestive symptoms of appreciable significance. They found 3 cases of gastric cancer, 2 of carcinoma and 1 of lymphosarcoma. All 3 cases were operable; all 3 lesions, resectable. There were no noted metastases. One patient who had carcinoma is still living after nine years; the second, who had carcinoma, died after six years, cause unknown; the patient with lymphosarcoma died of her disease shortly after surgery.

In 1945, Sherman*[,43,44] began using the same method on persons aged forty-five or over, and by 1949 had examined 2,858 persons with no gastrointestinal symptoms. He found 2 cases of gastric cancer. Both examinees were operable, both lesions resectable. There were no noted metastases. There was 1 patient with carcinoma, now living and well after four years, and 1 with myosarcoma now living and well after three years.

In 1947, we began the first attempt in this country to uncover unsuspected gastric cancer by photofluorographic methods, initially using standard camera equipment. Three carcinomas have been found. All examinees were operable; the 3 carcinomas were resectable. Two of the examinees had no lymph node metastases; they are living and well after twenty months and seven months, respectively; the third had a perigastric lymph node metastasis. He died of peritonitis. At necropsy, no residual cancer could be found.

In 1948, Roach, Sloan and Morgan[41] began using the photofluorographic method employing a Schmidt optical system, for the detection of gastric neoplasms. Although their work was not confined to a survey of symptom-free persons only, among the 10,000 examinations of dispensary patients aged forty or over, 5 persons either asymptomatic or with minor complaints were found to have gastric cancer. It is considered that they would ordinarily not have been referred for a regular gastrointestinal roentgen study.[42] All were operable. Resectability and metastasis rates and survival times are not given.**†

* Sherman also found one myosarcoma of the esophagus; the patient is now living and well after five years. In approximately an additional 2,000 studies since 1949 no other cancers have been uncovered.

** In 1945, Dailey and Miller[6] reported on the only other known purely roentgenologic approach to gastric cancer detection in this country; they examined 500 apparently healthy men aged forty-five or over. This work is not included in the summary above since they did not uncover any cancer.

† Five other photofluorographic gastric survey assemblies are present in the United States. It was hoped that data assembled from their operations could be included in this report. At the time of preparation of this paper, work with three of the units was either in a preparatory stage or had not begun.[17,27,56] One survey on about 2,500 examinees has proof pending on one or two neoplasms.[44] With the fifth installation, about 6,000 70 mm. examinations have been done, but no statistics are now available.[52]

For several years, the Minnesota group has been using a nonroentgenologic screening method for the detection of gastric neoplasms. Essentially, this consists of inserting various clinical and laboratory filters between examinees and possible conventional roentgenologic examinations, in order to reduce the load and the costs of the latter. Reports of this work have been published by Wangensteen,[54] State[45,46] and Rigler[39] with their co-workers. Their method has been very successful in uncovering concealed neoplasms. There have been 14 gastric cancers uncovered;[48] there were 7 with regional lymph node metastases and 7 with no metastases. The operability and resectability rates were 93 per cent.

This is a total of 23 cases of asymptomatic or unsuspected proved gastric cancers found in five different clinics,* some with different geographical locations, with medical and surgical staffs with possibly different conceptions of operability and surgical approaches. Nevertheless, for these people there is an operability rate of 95 per cent and a resectability rate of 95 per cent. The rate of apparent metastasis is 35 per cent (11 per cent for the four roentgenologic surveys). For the patients operated upon over three years ago, eight of twelve are still alive; of the five cases operated upon over five years ago, three are still alive. For the 23 cases, the projected five year survival rate** is forty three per cent (10 cases).

These figures can be compared with the following generally accepted rates, each rate being based on an initial 100 cases of diagnosed cancer, except the metastasis rate, which is necessarily based on operated cases only: operability—75 per cent; resectability for cure—25 per cent; metastasis—60 per cent; three year survival rate—10 per cent; five year survival rate—4 per cent.

Perhaps this seems to be a small number of cases of cancer, but on the basis of five year survival rates, it is equivalent to about 250 cases of symptomatic patients diagnosed and handled in the usual fashion.

This emphasizes for the early cancer, the one that is still in the latent period of its development, its enormously increased curability rate. Further support for the favorability of surgical attack on the early or small lesion is derived from Walters, Gray and Priestley[53] in whose series of 10,890 cases of carcinoma, 105 patients were subjected to the *least favorable* type of cancer surgery, local excision, but despite this, they had the highest survival rate—42.9 per cent! The median size of these lesions was 2.6 cm.

No further evidence is considered necessary to indicate that the surgical results with silent cancers is superior to those after symptoms have developed and metastases have gained ground, ending, after nevertheless prodigious labors, with about a 4 per cent five year survival rate.

There are several possibilities for developing methods for the early detection of gastric neoplasms. These are: (1) biologic tests, (2) roentgenoscopy, (3) clinical filters before conventional diagnostic roentgen procedures, and (4) photofluorography.

Considering these briefly, there has not been developed a reliable chemical or biologic test. As far as rapid roentgenoscopy is concerned, although the method is well known, it has not been adopted nationally because it has been considered hazardous and particularly because roentgenologist time consumption is too great. Concerning the work with clinical filters, the interposed filters themselves exclude far too great a portion of the population one would like to screen; there are too many persons with cancers of the stomach who have a normal or even a high gastric acidity. Further, the method is expensive, time consuming, and gastric intubation unpopular; and after all the preroentgenologic work is done *one-third* of the examinees still need conventional gastric examinations by roentgenologic means.[47]

The photofluorographic method need

* Hopkins cases excluded.

** This is based on the known metastases in these persons and the known survival statistics concerning metastasis.

have no limiting factors applied in the asymptomatic or relatively asymptomatic population, although practically, a lower age limit is applied. Further, it is inexpensive, rapid, accurate and popular.

Several features must be realized at the outset. One must not expect a high percentage of discovery of cases of cancer; that is, one must not be discouraged by a low incidence rate that abstract figures may induce. One must first be cognizant of the maximum attainment. This would be that of the known incidence of gastric cancer in symptomatic persons for any considered age and sex group.

Table 1 (after Dorn) establishes this.

TABLE I

INCIDENCE OF GASTRIC CANCER PER 100,000 WHITE POPULATION BY SEX AND AGE

Age	25–34	35–44	45–54	55–64	65–74	75 and Over	All Ages
Male	2	11	43	111	199	210	31
Female	1	7	20	56	90	148	16

In persons aged forty-five and over there is an average of 1.0 cases of gastric cancer in every 1,000 who are representative of the national age and sex distribution.

Second, one must release himself from the burden that if he is not doing the best he can (roentgenoscopy with roentgenography), he should do nothing.

Third, one must realize that this is not "photography" only, or a single film only, but a multiple and still reasonable nonhazardous number of planned films, and that *they are being used only as a screening device for conventional roentgenoscopy and roentgenography.*

Fourth, one must not assume that even with conventional methods we are infallible; and should realize that we do depend primarily on roentgenograms when we review those taken at examinations performed by our residents in training.

Fifth, one must recognize that neoplasms will be missed, just as when the standard study is performed, but that if the lesion has been silent no irreparable damage is done since the examinee would not have had a study anyway, will develop symptoms and the diagnosis can be established in the usual fashion; here one might insert that a roentgenologic mistake in a symptomatic person examined by conventional methods is worse, since this avenue to explain complaints may be lost.

Sixth, that the performance requirement of any cancer test is not expected to have 100 per cent positive results, or 0 per cent false positive tests.

And seventh, one may now know that the accuracy of this screening method is attested to by the facts: (1) that the number of neoplasms found is equal to and, in fact, slightly higher than by the two known and extensive roentgenoscopic approaches, relative age groups and sizes of groups considered; (2) that the number of cancers found in our survey is almost identical with the anticipated incidence of gastric cancer; (3) that the number of benign neoplasms found is not less than in most reports on general clinical material where both roentgenoscopy and roentgenography are employed; and (4) that the false negative error with the miniature films when these are checked by the standard study has been found in one experiment to be 1.4 per cent.[41]

THE JEFFERSON HOSPITAL STOMACH SURVEY UNIT

In the summer of 1947 the attempt to uncover gastric neoplasms by photofluorographic means was started. By September, 1947, Cancer Detection Centers in Philadelphia began to send their examinees to us, and these have been the primary source of suitable candidates. During the first two years the number of examinations done was

small, since the equipment used was an operating photofluorographic erect chest unit, and gastric survey studies had to be considered secondary to the chest examinations. By November, 1949, only 1,104 persons aged forty or over and considered free of significant symptoms had been examined. Up to this time no gastric neoplasms were found. However, during this period some patients, who during conventional roentgenoscopy in the regular department were found to have gastric cancer, were sent to the unit and it was apparent that at least moderate-sized neoplasms would register on the miniature erect films obtained with a Fairchild camera of standard type.

Subsequent to November, 1949, the work was transferred to a specially built and equipped room designated as the Stomach Survey Unit. A 70 mm. Schmidt-Helm camera with an equivalent f/number of 0.68 was employed.

The criteria for selection of a suitable candidate were that he be forty years or more of age and that he have no upper gastrointestinal tract symptoms of such nature that they particularly attracted his attention or that of his physician. To aid in determining the last point, the request form included the following question to be answered by the referring physician: "Would you have, in your personal practice, felt it necessary to refer this patient for a regular upper gastrointestinal study?" We considered that this category examinee was the practical one; that there are very few of us that do not at some time or another have occasional complaints; that the selection of totally asymptomatic persons would be too restrictive since the vast majority of persons fall in between the categories of totally asymptomatic and obviously symptomatic enough to require a regular gastrointestinal study. Tumors found in the group conforming to the stated requirement could truly be called silent and considered unsuspected.

During the eighteen months of operation with the imported camera, the total number of examinees studied has been increased to 5,341 and the total number of examinations to 7,075. This latter number includes periodic resurvey examinations as well as repeat examinations done because the preceding miniature films were unsatisfactory.

When the chest unit was used, the number of exposures was limited to three because of the relatively high number of roentgens to the skin.

The equipment used now is comparable to that described by Roach *et al.*,[40] with the exception that a Super Dynamax rotating anode tube is employed with an auxiliary fan to aid in heat dissipation.

The present positioning and barium sulfate technique is as follows: After the examinee swallows 1 ounce of barium sulfate mixture, he is placed prone on the table, rolled to the right oblique position to coat the antrum, and returned to a flat posture. Three exposures are made rapidly in the following sequence: posteroanterior, approximately 30° right anterior oblique, and next, one between 45° and 60° right anterior oblique. The examinee sits up, takes 5 additional ounces of the mixture and waits four to five minutes before the next exposures. These are taken rapidly in the following sequence: first and second, the same two oblique views as previously, and last, an anteroposterior exposure. The anteroposterior view at this stage allows for air contrast of the antrum and a portion of the corpus, and relatively complete barium distention of the fundus. The first three miniature films produce satisfactory delineation of the membrane pattern; the four oblique photofluorograms, a good idea concerning wall pliability and peristalsis.

The roentgenographic technical factors are: a tube-screen distance of 36 inches, employing 200 ma. with a potential of 95 kv. (peak), with the time photoelectrically controlled.

The total dosage at the skin, including backscatter, ranges between 4 and 12 r for the six exposures.

We believe that examinees should have such preparation that a minimum number of surveys will need to be done over because

of interference with food or excessive undergarments. Studies are made by appointment and preparation consists of the exclusion of food and fluids for at least six hours, and the precaution to wear no opaque undergarments. Because of the delay between the first three and last three exposures, ample opportunity is provided to correct clothing errors of the next person. The delay is necessitated because, without it, the first part of the duodenum will not be visualized in many persons. Although no effort is made to interpret the appearance of the duodenum, it is considered essential to fill it so that one is certain that the prepyloric antrum has been identified.

The interpretation report of the miniature films is made on the same form as the request blank so that all information is on one small sheet, and this sheet is primarily a system of checkmarks. If the presence of food is suspected, the examinee is returned for another study. If the antrum or duodenum is not well visualized, he is returned for another 70 mm. study with the noted instruction to the technician on the report form to increase the interval before the second three exposures to ten minutes. This increases the "unsatisfactory" group of examinations, but reduces the regular gastrointestinal roentgenologic examination load to an extremely practical level. Other unsatisfactory studies are repeated on the photofluorographic unit. Any person in whom an abnormality is suspected is returned for roentgenoscopic study and a minimum of at least spot roentgenography.

An analysis of those tested and studied is presented next.

Table II indicates the age and sex distribution of the 5,341 persons and is produced in the two forms commonly found in statistical literature.

It is to be noted that the ratio of females to males is 2.7 to 1 and that 54.5 per cent of the examinees are below fifty years of age. Both of these factors combined produce an unfavorable group to screen for gastric cancer. More comment will be made on this later.

TABLE II

AGE AND SEX DISTRIBUTION BY DECADE AND HALF-DECADE

Age	Females Number	Females Per cent of total females	Males Number	Males Per cent of total males	Total Number	Total Per cent
			Form I			
40–49	2,229	57.1	681	47.4	2,910	54.5
50–59	1,191	30.5	413	28.7	1,604	30.0
60–69	395	10.1	230	16.0	625	11.7
70–79	84	2.2	102	7.1	186	3.5
80–89	5	0.1	11	0.8	16	0.3
90–99	0	0	0	0	0	0
	3,904	100%	1,437	100%	5,341	100%
			Form II			
40–44	1,154	29.6	376	26.2	1,530	28.7
45–49	1,075	27.5	305	21.2	1,380	25.8
50–54	721	18.5	235	16.3	956	17.9
55–59	470	12.0	178	12.4	648	12.1
60–64	277	7.1	143	9.9	420	7.9
65–69	118	3.0	87	6.1	205	3.8
70–74	58	1.5	57	4.0	115	2.2
75 and over	31	0.8	56	3.9	87	1.6
	3,904	100%	1,437	100%	5,341	100%

Nonwhite examinees—299
Median age—Female— 48
Male— 50

Table III indicates the source of the examinees.

Although for the present experiment it

TABLE III

SOURCE OF EXAMINEES

Source	Number	Percentage
Cancer Detection Clinics	3,055	57.2
Self-referred	1,033	19.3
Jefferson Hospital Out-patient department	745	14.0
Private physicians	387	7.2
Jefferson hospitalized patients	84	1.6
Other (stores, etc.)	37	0.7
	5,341	100%

TABLE IV

NUMBER OF STUDIES PER VOLUNTEER

	Examinees	Examinations
1×	3,993	3,993
2×	1,003	2,006
3×	307	921
4×	35	140
5×	3	15
	5,341	7,075

TABLE V

EXAMINATIONS BY CAMERA TYPE

	Examinations	Per cent
70 mm. Schmidt-Helm camera	5,761	81.4
70 mm. Fairchild camera	1,314*	18.6
	7,075	100%

* For some time after the Schmidt-Helm camera was available, during breakdowns examinations were done on the Fairchild unit. At the present time, if persons do not desire to wait for repairs to be made, they are rescheduled.

was not originally intended to have self-referred persons come in, it could not be prevented since on two occasions newspapers gave the matter publicity. This necessitated some additional work for the Stomach Survey Unit since symptomatic candidates had to be excluded by our members. We have reasonable assurance that even this group conforms to our original decision concerning the acceptability of candidates.

Table IV indicates the number of times any single one examinee was studied by the photofluorographic technique and Table V indicates the type of camera employed.

Most of the persons who were originally examined with the Fairchild standard photofluorographic camera returned for periodic examinations after the Schmidt optical system was installed. Analysis of this point indicated that only 538 examinees were studied with the Fairchild camera alone.

Table VI lists the studies which were considered satisfactory or unsatisfactory from a screening standpoint, and Table VII separates the reasons that the camera techniques were unsatisfactory. Also listed is the final outcome in these cases.

TABLE VI

QUALITY OF PHOTOFLUOROGRAPHIC STUDY

	Number of Examinations	Per Cent
Satisfactory	6,566	92.8
Unsatisfactory	509	7.2
	7,075	100%

TABLE VII

UNSATISFACTORY PHOTOFLUOROGRAPHIC EXAMINATIONS

First Study Cause	Repeated Study Satisfactory	Repeated Study Unsatisfactory	Third Study* Unsatisfactory	Lost to Follow-up	Total
Antrum not distended or bulb not seen	155	1	1	7	
Camera: jams or out of focus	121			4	
Development errors	102	2	2 (camera jams)	3	
Food	60			1	
Obesity	15			7	
Other (positioning, breathing, clothing)	23	1 (bulb not seen)		4	
	476	4	3	26	509

* The present policy is that if two successive photofluorographic studies are unsatisfactory, a regular gastrointestinal examination is recommended, regardless of cause.

The percentage of unsatisfactory studies is slightly less than that reported in a purely roentgenoscopic survey as either unsatisfactory or of limited value—9.5 per cent.[43]

There is every reason to believe that experience is reducing some of these difficulties in this unsatisfactory group and that new cameras being manufactured will reduce the number of jams.

Table VIIIA indicates the interpreted status of the stomach on the miniature films in the satisfactorily exposed group of *studies* as well as the disposition of the study for the immediate period. Table VIIIB indicates the disposition of the *examinees*.

TABLE VIIIA

DISPOSITION OF STUDY IN SATISFACTORY EXAMINATIONS

	Number	Per Cent
Negative for neoplasm (study closed for period)	6,244	95.1
Regular gastrointestinal examinations recommended	322	4.9
	6,566	100%

TABLE VIIIB

DISPOSITION OF EXAMINEE AFTER PHOTOFLUOROGRAPHIC EXAMINATION

	Number	Per Cent
Negative for neoplasm (case closed)	4,993	93.5
Regular gastrointestinal examination recommended	322	6.0
Lost to follow-up	26	0.5
	5,341	100%

In considering the total number of recommended standard studies, it is felt that, practically, the percentage should be based on the number of satisfactory miniature examinations rather than the total number of examinees, for in a sense the person returning for a periodic re-evaluation constituted another individual for whom a comparable decision had to be made.

There were numerous non-neoplastic conditions diagnosed on the 70 mm. evidence alone. These are listed in Table IX.

TABLE IX

NON-NEOPLASTIC CONDITIONS

Hiatus hernia, including intrathoracic stomach	138
Deformed duodenal bulb	42
Duodenal diverticulum	36
Gastroenterostomy	6
Cholelithiasis	3
Stag-horn renal calculi	2

Other conditions such as enlargement of the spleen, liver, kidney and heart were reported. Anomalous gastric positions were noted. There were 38 questionable or probable hiatus hernias noted; these are not included in the group of definite ones listed above. Several bone changes were apparent as well as a calcified fibroid.

In regard to the duodenal bulb, no effort was made to give a conclusive opinion except in the 42 cases in which the deformity was so marked or the change so constant on several films that no doubt existed. Possible activity, as far as an inflammatory lesion is concerned, was only inferred on 3 occasions on the basis of photofluorographic appearance alone.

There were 322 examinees, on whom, because of the photofluorographic findings, we recommended standard gastrointestinal studies.

In 286 of these instances, the studies can be considered as closed; there were no changes suggestive of gastric neoplasm on the standard examination. The changes on the photofluorograms which led to the recommendation of a conventional study and the learned or probable accountable factor noted while doing the conventional study, are listed in Table x. The table is divided into two sections: the first section includes the examinations done on candidates who can be considered as well; the second section outlines 24 conventional examinations done on persons considered as symptomatic.

TABLE XA

REASONS FOR RECOMMENDING STANDARD GASTROINTESTINAL STUDY ON GROUP OF WELL PERSONS

Reason	Number of Cases	Per Cent	The Learned or Probable Accountable Factor
1. Antrum not well distended or visualized, or duodenal bulb not visualized	90	34.3	None, other than poor filling, 68; pylorospasm and antral spasm, 11; goose-neck antrum, 5; duodenal ulcer, 2; elongated pyloric channel, 2; gastroenterostomy, 2
2. To exclude antral polypoid mass	46	17.6	None, 28; heavy rugae, 9; food, 6; artefact, 2; goose-neck antrum, 1
3. To exclude significant fundus abnormality	28	10.7	None, other than poor distention by air or barium, 18; small hernias, 4; cardiac imprint, 3; splenic flexure, 2; costal cage, 1
4. To exclude tumor from corpus	20	7.6	None, 8; local area of poorly defined rugae, 5; food 4; costal cage, 2; artefact, 1
5. Indented or flattened prepyloric lesser curvature or other antral deformity	16	6.1	None, 10; heavy folds, 3; previous surgery or ulcer, 2; food, 1
6. To exclude greater curvature polypoid lesions or irregularities	14	5.3	None, 5; heavy rugae, 2; colon pressure, 2; food, 1; gastroenterostomy, 1; costal cage, 1; spleen, 1; splenic flexure, 1
7. To exclude gastric ulcer	13	5.0	Peristalsis, 6; heavy rugae, 3; overlying small bowel, 2; none, 2
8. Generalized polypoid pattern or enlarged rugae	8	3.1	Heavy rugae, 4; food, 2; none, 1; chronic gastritis (gastroscopic biopsy), 1
9. Deep incisuras	5	1.9	Probably normal peristaltic effect, 5
10. Other gastric changes	6	2.3	None, 5; food, 1
11. Nongastric changes. To exclude significant disease or to confirm minor benign changes in esophagus and small intestine	16	6.1	Short esophagus (with gastric hernia), 3; diverticulum of esophagus, 2; cardiospasm, 1; duodenal diverticulum, 2; megabulb associated with anomaly of loop, 2; other, 2; none, 4
	262	100%	

TABLE XB

REASONS FOR RECOMMENDING STANDARD GASTROINTESTINAL STUDY ON GROUP OF SYMPTOMATIC PERSONS

Reason	Number of Cases	The Learned or Probable Accountable Factor
1. Antrum not well distended or visualized, or duodenal bulb not visualized	6	None, other than poor filling, 4; pyloric channel ulcer, 1; prolapsed membrane and deformed bulb, 1
2. To exclude gastric ulcer	4	None, 2; peristalsis, 1; clothes, 1
3. To exclude significant fundal abnormality	4	None, other than poor distention by air or barium, 4
4. Deformities probably due to food	2	Food, 2
5. To exclude antral polypoid mass	1	Heavy rugae, 1
6. To exclude greater curvature polypoid lesion	1	Heavy rugae, 1
7. Food on 2 occasions	1	Food, 1
8. Irregular lesser curvature	1	None, 1
9. Pyloric channel ulcer, with possible gastric ulcer	1	Gastric and pyloric channel ulcers, 1
10. Nongastric changes. Achalasia; probable duodenal ulcer	3	Achalasia, 1; active duodenal ulcer, 1; deformed bulb, 1
	24	

These 24 standard procedures were ordered on a total of 245 symptomatic persons in the entire surveyed group. Although their inclusion in this experiment was not considered desirable, it occurred through initial uncertainty on the part of some of the referring physicians as to who could be considered a suitable candidate. To continue to encourage good will from our very satisfactory referring agencies, it was considered poor policy to turn these persons down after they had prepared themselves for the examination and arrived at the Survey Unit door.

There are 8 additional cases for whom we have recommended regular upper gastrointestinal examinations, but they have not been done and the photofluorographic studies must be considered as not followed up. The remaining 28 cases are subdivided into three groups.

The first group consists of 3 examinees who were operated upon on the basis of our recommendations following conventional roentgenologic examination, and in whom there was no surgical or pathologic evidence of neoplasm. None had any symptoms referable to the stomach. The first patient, a white man, aged fifty-five, had a very heavy rugal pattern along the greater curvature with what was considered as evidence of a greater curvature ulcer. He was studied extensively at another hospital, where again surgery was recommended. At laparotomy, the stomach was considered normal to palpation, and gastrotomy was not performed. He is living and well three years later; presumably no cancer was present. The second patient, a white man, aged seventy-two, had a very narrow prepyloric segment with no evidence of peristalsis on either curvature for a distance of 2 cm. No membrane pattern was discerned in this area. During operative preparation, when the patient was under anesthetic effect, a mass could be palpated through the abdominal wall. The resected specimen demonstrated marked muscular hypertrophy of the pylorus and antrum. He is living and well after one and one-half years. The third patient was a white woman, aged fifty-five, in whom the rugal pattern along the greater curvature was unusually heavy and in whom on three occasions one could reproduce a polypoid lesion about 1 cm. in size. Although it was first considered that she might be watched, when it was determined that she was achlorhydric, it was thought preferable to do a laparotomy. At gastrotomy, it was evident that a finger-sized rugal fold running transversely across the greater curvature in the pars media accounted for the change. The histopathology was chronic gastritis with glandular hypertrophy. She is living and well after three months.

The second group of remaining cases consists of 13 persons whose records have not been closed since we desire to follow them further for years. Some of these examinees were first studied in 1948. The lack of progressive changes over long intervals suggests that the lesions cannot be considered as neoplastic and surgery has not been recommended for any of these examinees. On the other hand, since most have antral disease, and since there is some evidence that lesions such as gastritis may be precursors of cancer, it is considered safer to keep these persons under periodic observation. Only 1 of the 13 has symptoms which would warrant conventional study. In each case the area suspected of being abnormal on the photofluorographic films is the area under consideration now. There is 1 case of gastric ulcer which healed under medical therapy and has remained healed for seven months. There is another case in which we think a 2–3 mm. polypoid pedunculated tumor may be present but, since this is so small and since it may be merely a mucosal tab, we consider it preferable to re-examine her after a suitable interval. In this one instance, although a radiotranslucent defect was present in the same region on the miniature films, the defect was larger than that under observation now, and was probably nonspecific. The other 11 examinees have membrane changes, either in size or pattern distortion, with and without pyloric and antral constrictions and local peristaltic disturbances. They can prob-

ably be classified as cases of chronic gastritis, possibly some with muscular hypertrophy.

In 1 of these persons, conventional roentgenography disclosed that the lower pole of a kidney was markedly enlarged and contained a streak of calcium. The surgical specimen was a hypernephroma. This renal cancer was an asymptomatic one. No metastasis has been discovered and the patient is alive and well after eleven months. Although the abnormal kidney shadow was not noted during the interpretation of the miniature films, retrospectively it is obvious (Fig. 1).

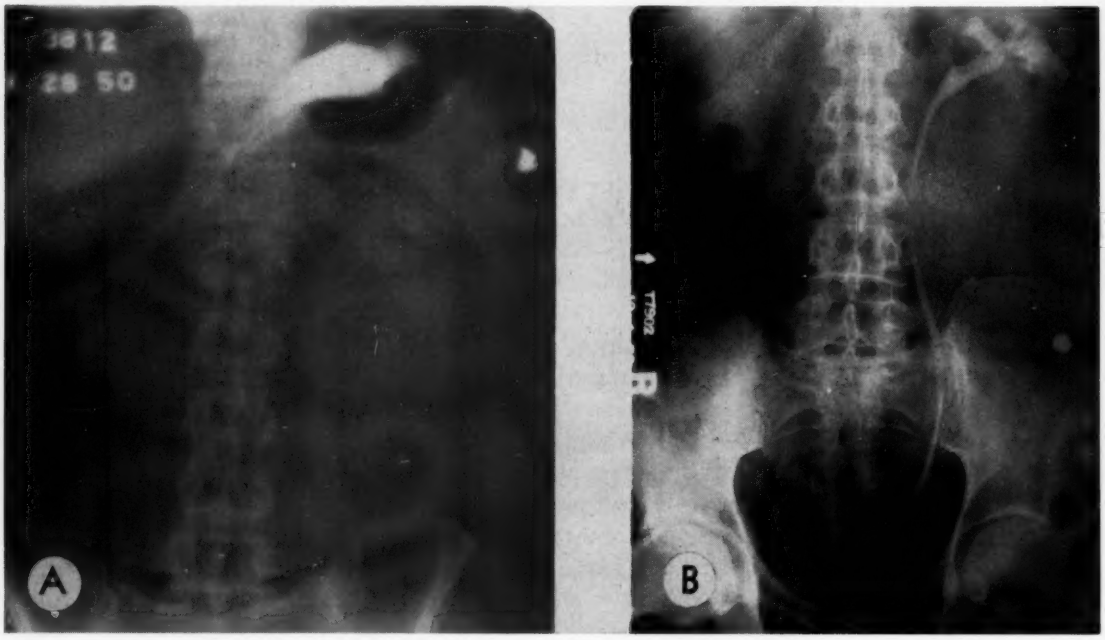

FIG. 1. (*A*) Photofluorogram demonstrates enlarged kidney. (*B*) Retrograde pyelogram demonstrates a large renal mass (asymptomatic hypernephroma).

The last group of examinees consists of 12 cases in whom gastric neoplasms were uncovered. One patient was definitely symptomatic and would have had a regular conventional study ordered. He had a nonresectable carcinoma of the stomach with extension to local lymph nodes, the pancreas and the liver.

We consider that in the final 11 cases the neoplasms can properly be categorized as silent tumors. Three (1 carcinoma, 2 adenomas) were discovered on repeat photofluorographic examinations, the initial studies being unsatisfactory. In 2 instances the stomachs had contained food and in 1 instance the films were technically unsatisfactory. Only 1 tumor was discovered among the 1,225 periodic resurvey examinations. An erect study on this examinee made in 1948 with the Fairchild chest camera is retrospectively considered as negative, although excessive barium in the antrum could have concealed the adenoma. A recumbent study in February, 1950, with the Schmidt-Helm camera retrospectively shows equivocal evidence of the presence of the small lesion. The regular study was ordered on the basis of a 70 mm. recumbent survey examination done in December, 1950. Therefore, it is not known whether the tumor was overlooked or developed during the interval.

The 11 cases of silent neoplasm are summarized in Table XI and their appearances on both the photofluorographic films and conventional roentgenograms are shown in Figures 2 to 12.

TABLE XI

SUMMARY OF EXAMINEES WITH CONCEALED GASTRIC NEOPLASMS

Age	Sex	Race	Source	Roentgenologic Appearance	Surgery	Histopathology	Follow-up
45	F	W	Cancer Detection Clinic	4 cm. ulcerated carcinoma	Resected. No metastases	Carcinoma (unclassified)	Living and well, 1 yr., 8 mo.
63	F	W	Private physician	3 cm. polypoid neoplasm	Resected. No metastases	Adenoma with adenocarcinomatous change	Living and well, 7 mo.
65	M	W	Self-referred	4–5 cm. carcinoma	Resected. One perigastric node with metastasis	Adenocarcinoma	Died postoperatively of peritonitis. Postmortem—no residual cancer
49	F	W	Cancer Detection Clinic	1.5 cm. polypoid neoplasm	Excised. No metastases	Grossly, benign adenoma. Tissue lost	Living and well, 10 mo.
47	F	C	Out-Patient Department	2–3 polypoid neoplasms; largest 1 cm.	3 neoplasms excised. No metastases	Benign adenomas	Living and well, 10 mo.
63	F	W	Cancer Detection Clinic	1 cm. polypoid neoplasm	Excised. No metastases	Benign adenoma	Living and well, 7 mo.
67	F	W	Cancer Detection Clinic	1.5 cm. polypoid neoplasm	Excised. No metastases	Benign adenoma	Living and well, 3 mo.
69	M	W	Out-Patient Department	8 mm. polypoid neoplasm	Excised. No metastases	Benign adenoma	Living and well, 2¼ mo.
55	M	C	Out-Patient Department	4–5 cm. polypoid neoplasm, infiltrative	None. Inoperable: cardiovascular disease, severe	Unknown. Possibly malignant	Being followed
55	F	W	Out-Patient Department	Multiple polypoid neoplasms; one considered infiltrative	None. First accepted; later refused	Unknown. Possibly malignant	Being followed
46	F	W	Cancer Detection Clinic	7 mm. polypoid neoplasm	Refuses surgery. Gastroscopy: probably benign "polyp"	Unknown	Being followed

It is interesting and significant to note that had we closed out the studies on examinees with unsatisfactory photofluorograms because of the presence of food or technical difficulties we would have permitted 1 carcinoma and 2 benign adenomas to go by undetected. It seems to us that once having committed oneself to the survey of these persons, there is a moral obligation to make every effort to repeat unsatisfactory survey examinations.

A very practical consideration arises concerning periodic resurveys. Only 1 neoplasm was found in the 1,225 examinations done; the majority of these were done after an interval of but one-half year and a year. This ratio is to be contrasted with the 10 tumors found in the other 5,850 examinations. Although too few periodic surveys were done to predict categorically what the case-finding percentage would be, or what the most productive interval for restudy should be, the trend toward a longer interval is at least suggested. Also, the case-finding rate is indicated as being greater among new examinees and probably will be among examinees done not more frequently than each two years. Surveys done on a national scale with a two year interval between examinations would be less expensive and, as will be indicated later, practical on a professional basis.

Although all possible clinical gastric studies were not done on these persons with gastric neoplasms, and although it is not the purpose of this paper to present all of those that were done, it is interesting to point out that if we had interposed the filter of a required low gastric acidity for the examinees who had conventional studies ordered, *before the study would be carried out*, we would have excluded at least one gastric carcinoma, and probably a second. The latter examinee was hyposecretory to an Ewald meal but probably would have been isosecretory to histamine stimulation.

By photofluorographic screening methods, then, 11 gastric tumors were found in 5,096 persons aged forty or over who were either totally asymptomatic or were free of

appreciably significant gastrointestinal complaints. The incidence of unsuspected neoplasms is 2.1 per 1,000 examinees; the incidence of unusupected gastric carcinoma, 0.6 per 1,000. In the examinees forty-five years of age or more, these incidences per 1,000 are 3.0 and 0.8, respectively. In the group aged fifty or over, there were 7 neoplasms, 2 of which were carcinomas. In these persons the incidence for neoplasm is 3.0 per 1,000 and for the carcinomas, 0.9 per 1,000.

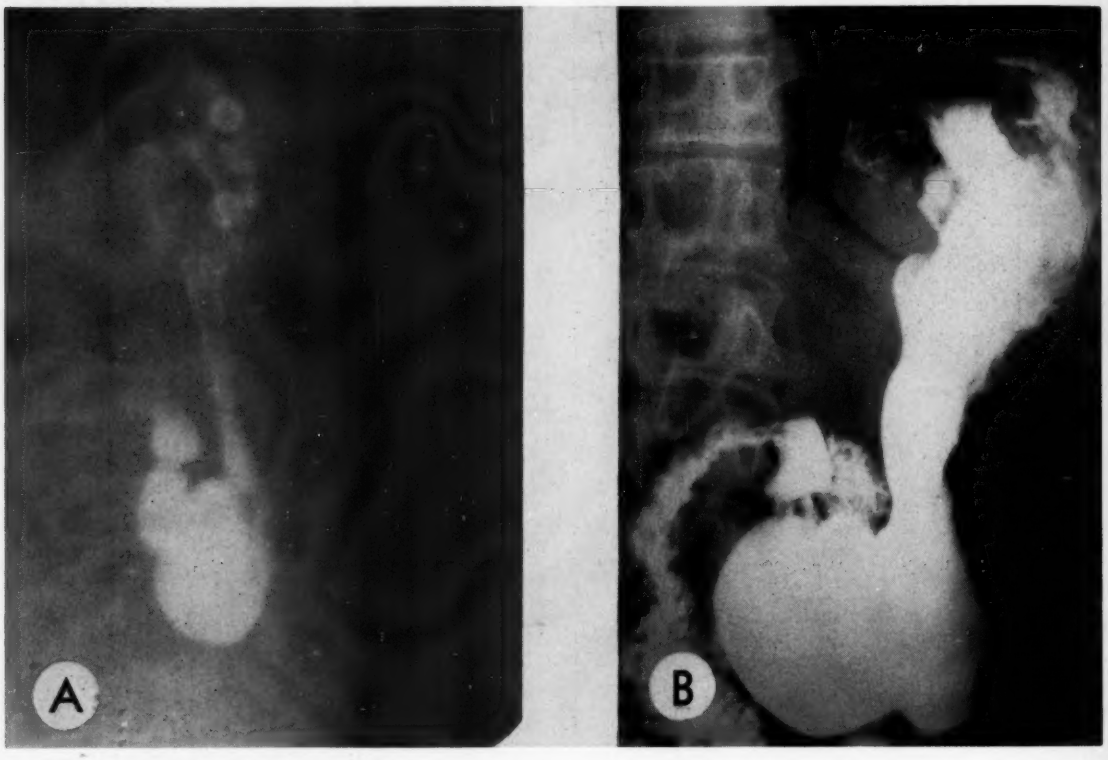

FIG. 2

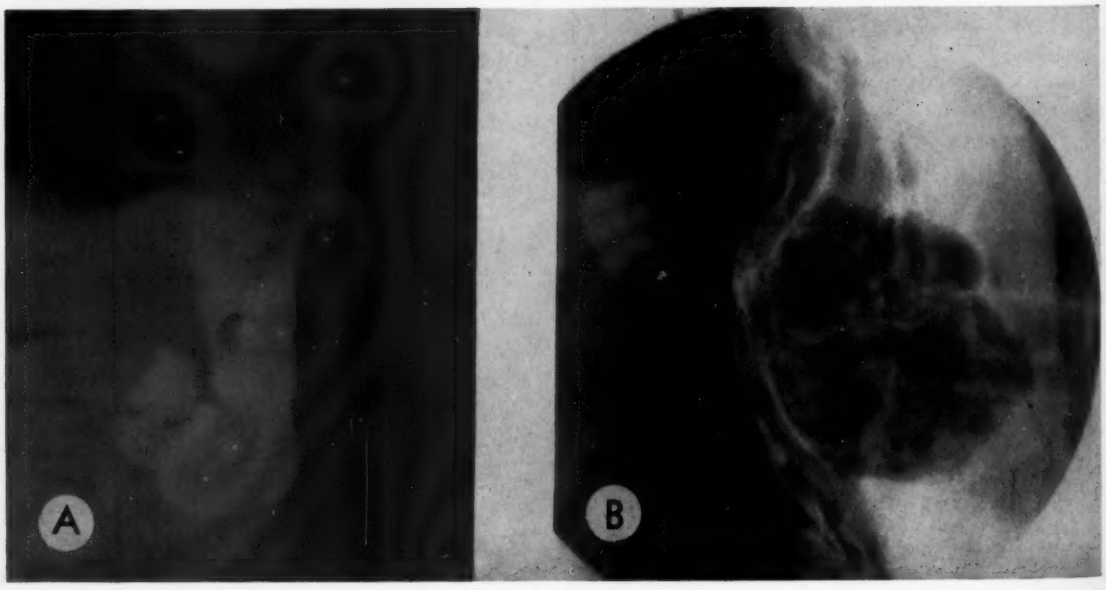

FIG. 3

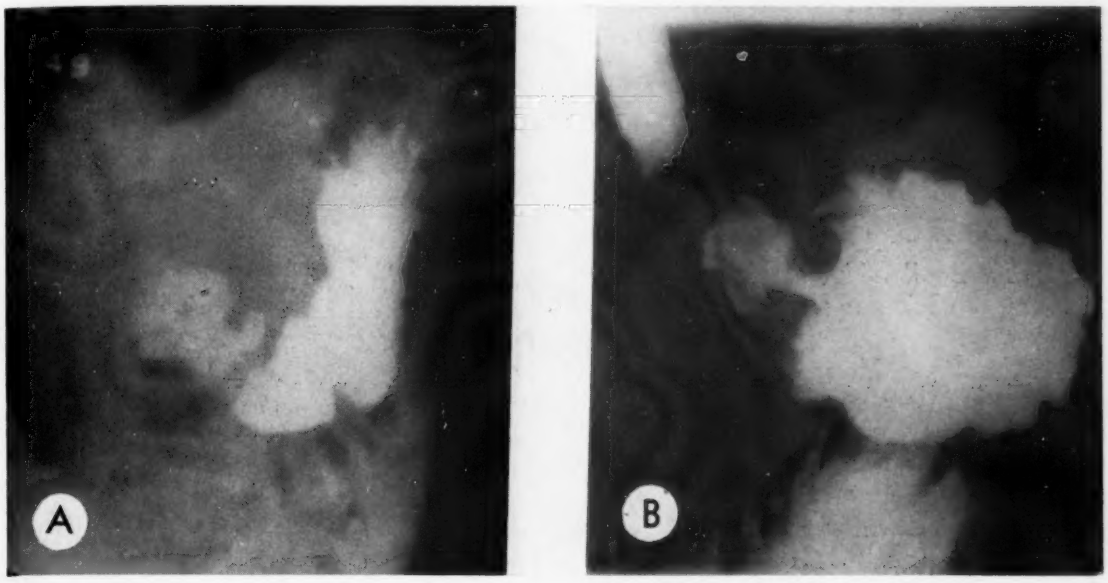

Fig. 4

Fig. 2–4. (*A*) Photofluorograms and (*B*) conventional roentgenograms demonstrating 3 cases of gastric carcinoma.

This survey unit screened 6,566 satisfactory studies down to 322 recommended conventional roentgenologic examinations, or less than 5 per cent. The various filters used in the screening techniques practiced by the Minnesota group, both clinical and laboratory in type, reduces the numbers of standard studies to but 33 per cent.

The 11 gastric neoplasms were found in 3.4 per cent* of the regular studies ordered; stated in another fashion, we found 1 neoplasm in every 30 standard gastric examinations. This figure is quite comparable to that attained in general roentgenologic work! It is so, not because of the numbers of carcinomas found, but because of the large number of polypoid tumors uncovered.

Gastric "Polyps"

The detection of gastric "polyps," particularly adenomas, seems to us to bear almost equal significance to that of the discovery of silent gastric cancers. Sherman's work, together with ours, comprising about 10,000 examinees, would suggest that adenomatous polyps will be found in the ratio of about 3 adenomas to each frank gastric cancer. Although this has no *immediate* effect on the salvage rate for gastric cancer, the extirpation of these precursors of carcinoma will *ultimately* significantly reduce the incidence of malignant neoplasms, when surveys are done on the greater portion of the national population in the tumor-bearing ages.

Unfortunately, it is difficult to establish how many gastric adenomas are malignant from the beginning or how many become malignant. It is evident that if an adenomatous polyp is malignant, it will be classified in pathologic language as a carcinoma and in the reported literature its identity as an adenomatous lesion is obscured by the descriptive term applied to the malignancy. Further not all gastric polypoid tumors are studied microscopically, particularly in postmortem material. Since only recently has real attention been paid to this tumor, when a small neoplasm, grossly fitting the loosely applied term of "polyp" is submitted for section, it appears so be-

* This percentage is slightly greater if the conventional examinations recommended on the persons lost to follow-up and also those done on the symptomatic cases are excluded.

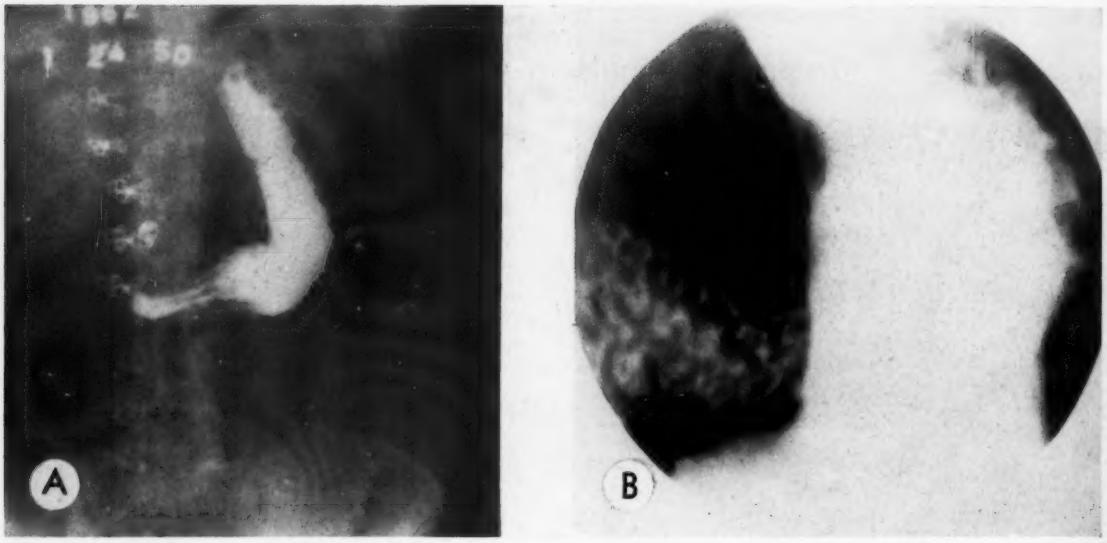

FIG. 5

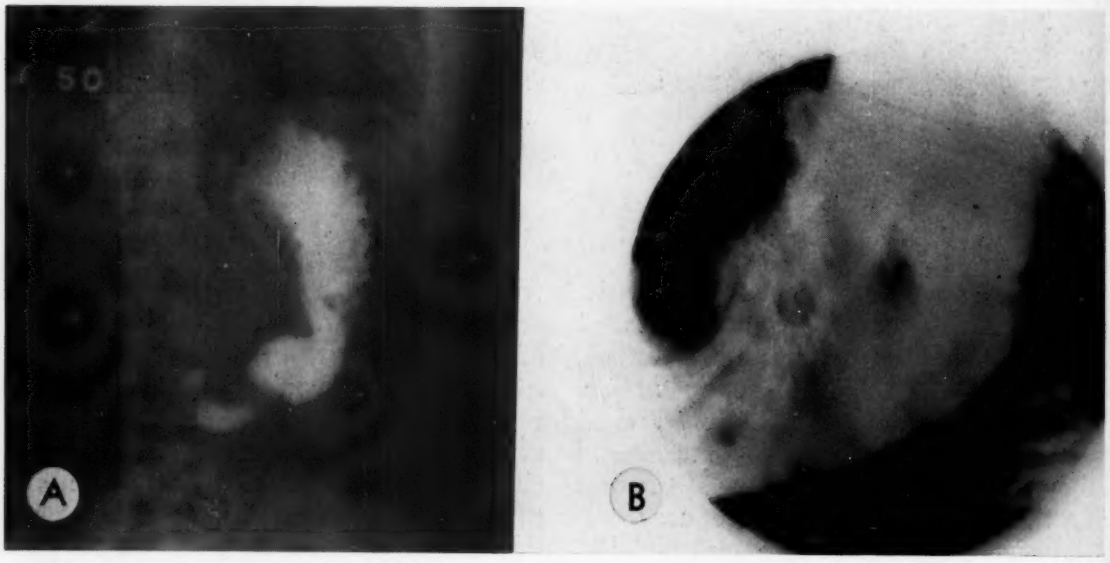

FIG. 6

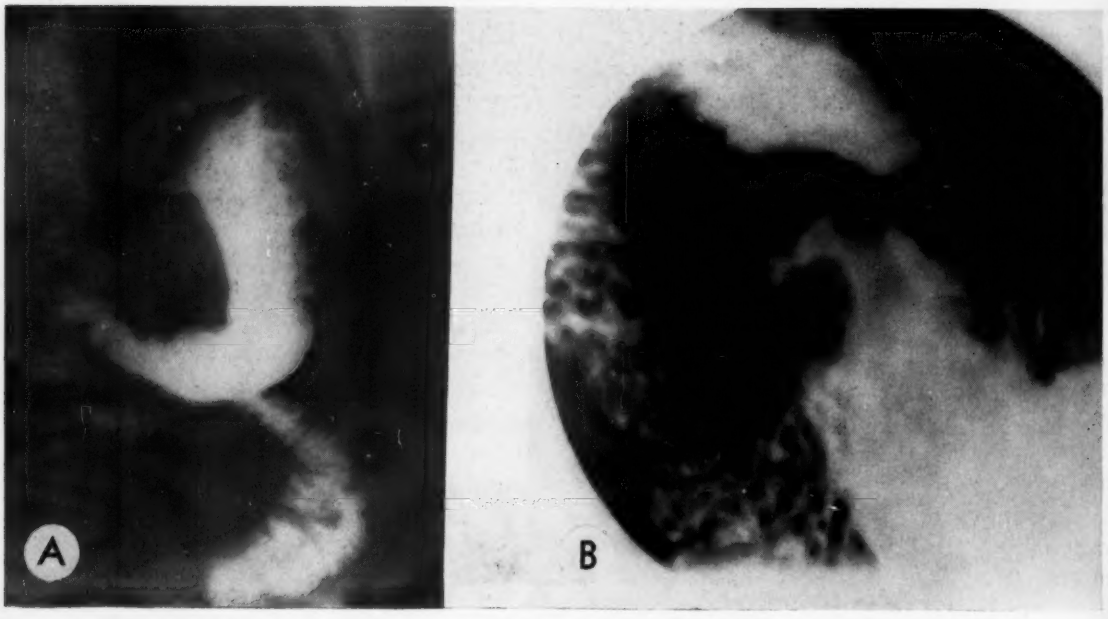

FIG. 7

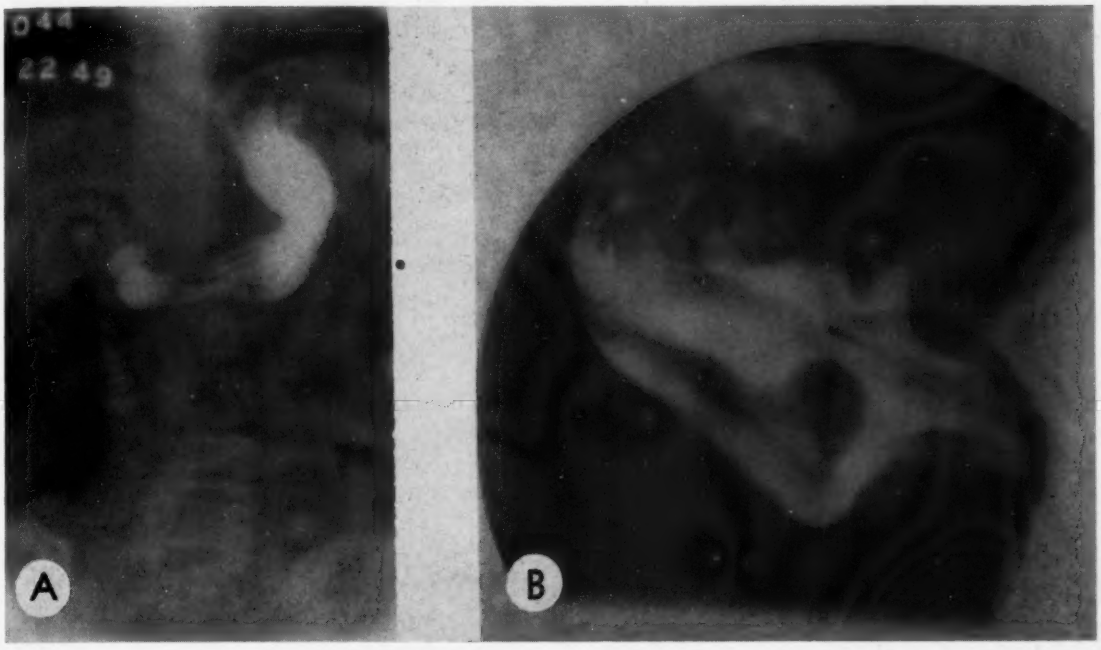

FIG. 8

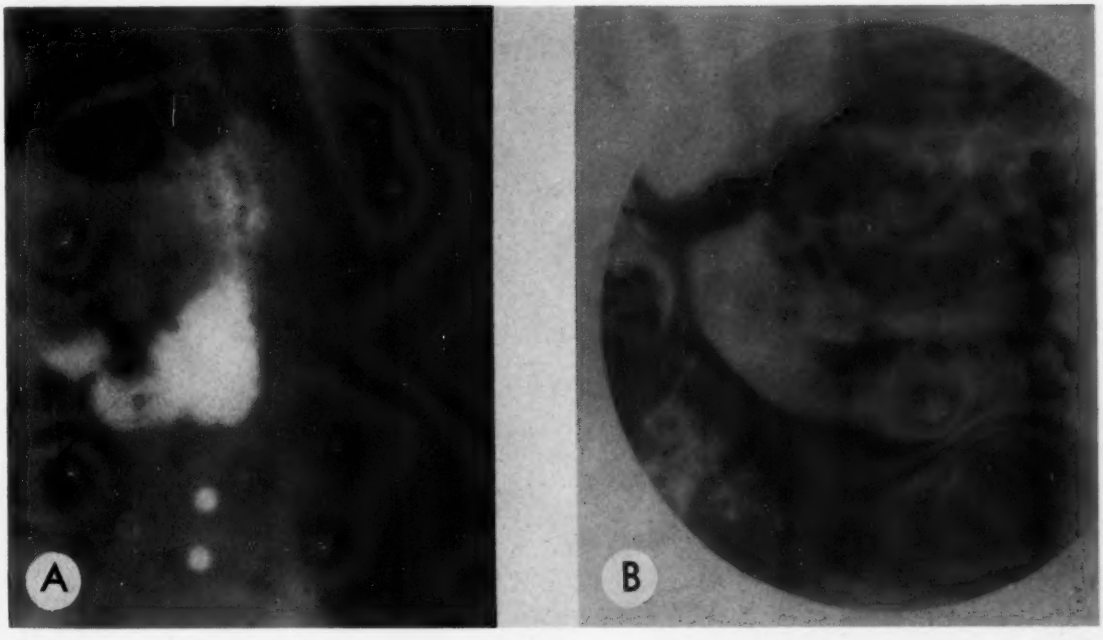

FIG. 9

FIG. 5–9. (*A*) Photofluorograms and (*B*) conventional roentgenograms demonstrating 5 cases of single and multiple benign adenomas.

nign that only infrequently are serial sections done to search for the earlier cellular changes of beginning malignancy. Another major feature is that not all pathologists have equal regard for minor cytologic detail and so their appreciation of such changes as might be called "carcinoma in situ"[32] varies considerably.

The following rates of incidence are known. (Where the unqualified term "polyp" or benign tumor is shown, it can be considered that a large portion are adenomas.)

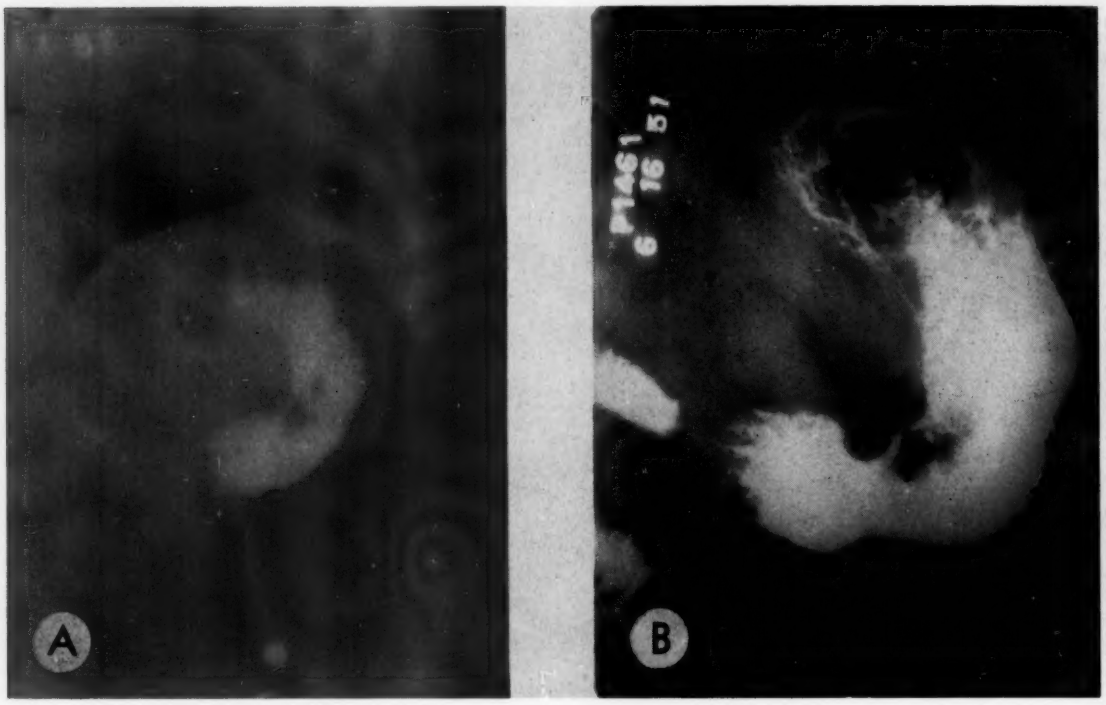

FIG. 10. (*A*) Photofluorogram and (*B*) conventional roentgenogram demonstrating polypoid neoplasm, type unknown.

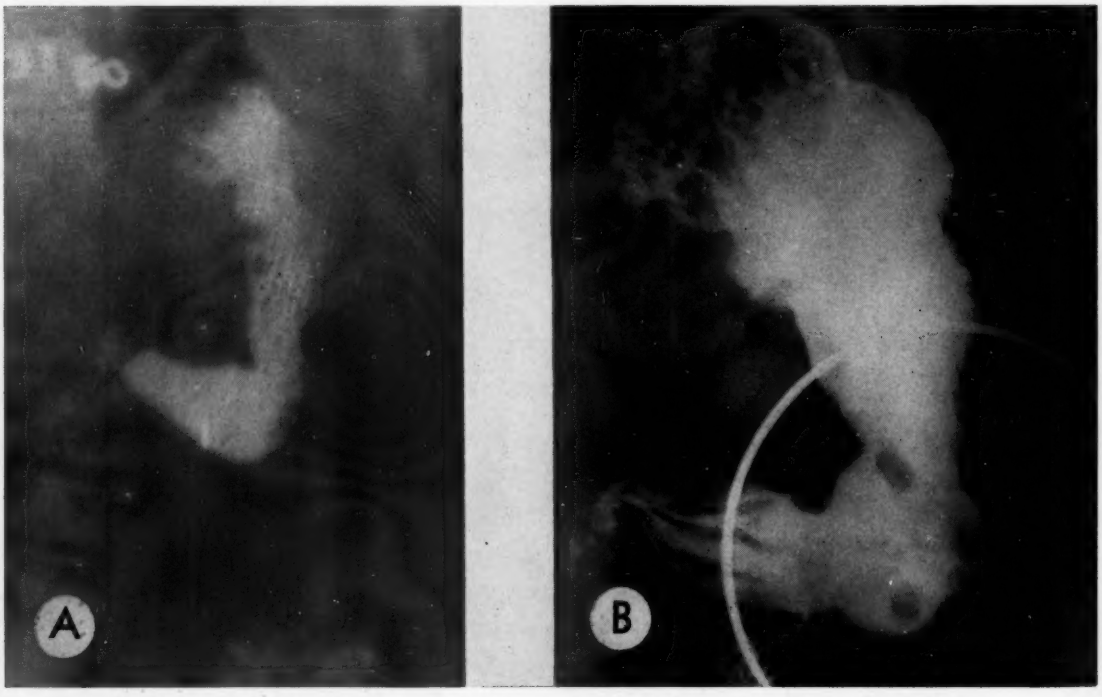

FIG. 11. (*A*) Photofluorogram and (*B*) conventional roentgenogram demonstrating multiple polypoid neoplasms.

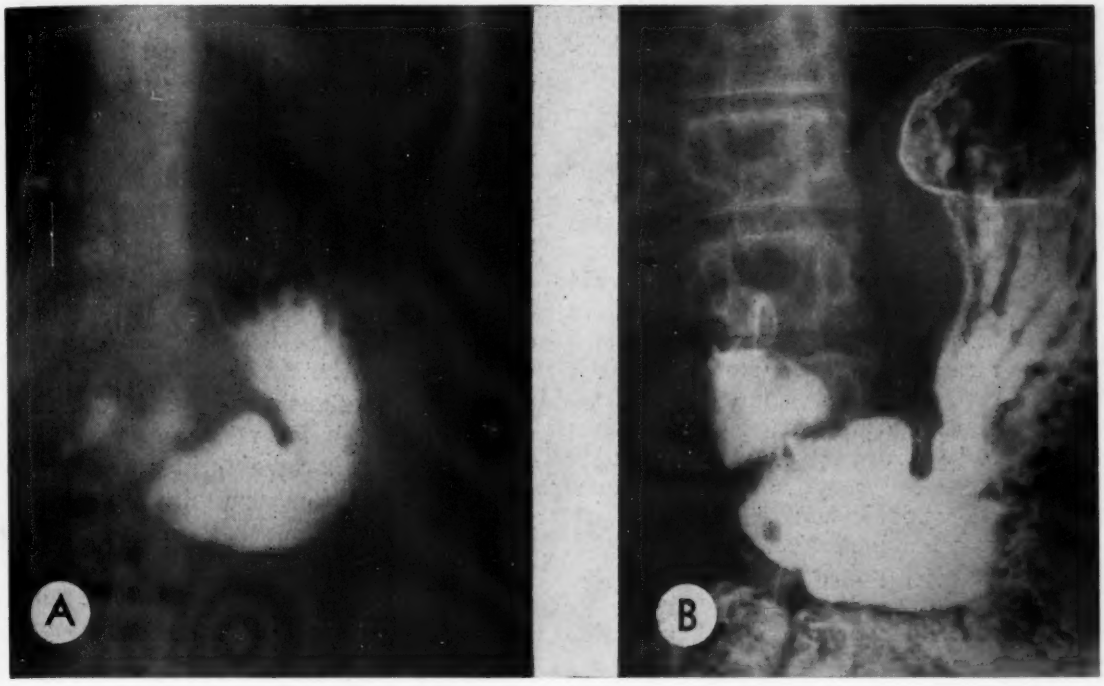

FIG. 12. (*A*) Photofluorogram and (*B*) conventional roentgenogram demonstrating a single small polypoid neoplasm, type undetermined.

(a) Survey studies:
  (1) Population not suspected of harboring neoplasms.
    Hauser—A 1 cm. "polypoid lesion," adenocarcinoma, in 100 examinees aged forty or over.
    St. John, Swenson and Harvey—1 "polyp" in 2,413 examinees aged fifty and over.
    Sherman—6 adenomas in approximately 2,858 examinees forty-five years old and over. (In an estimated 2,000 additional studies several more "polyps" have been found.)
    Dailey and Miller—1 suggestive "polyp" in 500 examinees (men) forty-five and over.
    Present Authors—1 adenoma with carcinomatous change.
      5 benign adenomas, single and multiple, proved.
      1 multiple polyposis, undoubtedly adenomatosis, histopathology not ascertained.
      1 sessile polypoid neoplasm, possibly carcinoma, not ascertained.
      1 "polyp," possibly benign adenoma, histopathology not ascertained, gastroscopically verified.
    (These neoplasms were found in the 3,811 examinees aged forty-five or over.)
  (2) Hospital population, symptomatic and asymptomatic.
    Roach, Sloan and Morgan—10 "polyp or polypoidlike filling defects," character unproved, and 1 "polyp," 1 multiple polyposis, 1 leiomyoma and 1 neurofibroma proved among 10,000 out-patients. The greater portion of these 14 cases had absent or minimal symptoms.
(b) Conventional studies:
  Dwyer and Blackford[11]—3 benign tumors (1 multiple polypi) in 3,000 symptomatic cases.
  Kirklin and Weber[24] and Kirklin and Hodgson[25]—1 benign tumor in about 2,000 hospital and clinic patients.*
  Rigler and Ericksen[38]—21 benign tumors and 4 "benign tumors with malignant degeneration" in 4,236 symptomatic

* Estimated on the basis of the two papers.

cases. (Probably large numbers of patients with pernicious anemia and achlorhydria.)

(c) Filter studies preceding conventional roentgen examinations:

State *et al.*[46]—42 "polyps" in 1,544 patients with achlorhydria and hypochlorhydria.

4 "polyps" in 94 patients with pernicious anemia.

2 "polyps" in 1,715 persons in *good health* over age forty-five who had various filters interposed before 312 standard roentgen studies. (Note that this group, which also included 1 carcinoma, is representative of populations to be surveyed; it is the one to compare with groups surveyed by photofluorographic methods.)

(d) Necropsy studies:*

Steiner[50]—63 gastric "polyps" in 8,000 autopsies.

Stewart[51]—56 gastric "polyps" in 12,800 autopsies.

Lawrence[28]—50 gastric adenomas in 7,000 autopsies.

Eliason and Wright[12]—37 gastric "polyps," adenomata and papillomata, in 8,000 autopsies.

It is therefore indicated that gastric adenomas are in no sense of the word rare and also that their discovery by photofluorographic means at least appears as good as by the standard method; this seems so, even excluding the fact that in the conventional studies many of the larger tumors were probably symptomatic, a point which makes such groups more select.

The following percentages are quoted to indicate what portion of all gastric neoplasms are benign.

(a) Clinical material:
Kirklin and Weber—2%
Eusterman and Senty[14]—1.3%
Dwyer and Blackford—3.2%

(b) Surgical and necropsy studies:
Lockwood[29]—4.3%

(c) Necropsy studies; carcinomas and adenomas, only:
Stewart—14.8%
Rigler and Ericksen—19.3%

* The higher incidence of "polyps" at autopsy is accounted for by: (1) open inspection is more satisfactory than roentgenographic; (2) median age is higher; (3) the pathologist is viewing the summation of the growth potential of the gastric membrane, not its potential after any one segment of the life span.

The fact that adenomas are found with such greater frequency than carcinomas in surveys on asymptomatic or relatively asymptomatic persons and with such considerably less frequency than carcinomas in symptomatic patients would imply that many carcinomas are founded on an adenomatous basis.

The fact that one large clinic (Mayo Clinic) must do 100 conventional gastric examinations to find 2.4 carcinomas and that they consider that about 2.0 per cent of gastric tumors are benign indicates that they do about 2,000 roentgenoscopic and roentgenographic examinations to find one benign tumor. Now, one may ask himself why there are not more benign tumors found in the symptomatic (hospital) population. It is not reasonable either to assume that symptoms protect one from adenomas or to presume that the standard study is so much poorer than the photofluorographic one. The only reasonable answer is that by the time some persons become patients, that is, part of a hospital population, their adenomas have become carcinomas!

Is it reasonable to assume that the incidence of both benign and malignant neoplasms, best determined in a nonsuspect group, changing so dramatically in necropsy studies, can be accounted for merely by saying that so many of the sick die of gastric cancer in hospitals, that this must be the only accountable factor? We prefer to think that part of this change is accounted for in the same fashion as above; that some of the cancers have developed from adenomatous precursors; that a secondary carcinoma may be so large as to have concealed the characteristics of the original tumor.

The following further evidence is presented.

The transformation of a gastric "polyp" to a carcinoma has been described.[26]

Tumors described by pathologists as benign adenomas have recurred subsequently and been described as malignant.[4]

The frequency of malignancy in "polyps" is greater in the age over sixty.[4]

The greater frequency of both adenomas and carcinomas in patients with pernicious

anemia indicates a comparable biological predeterminism.

Stewart found single or multiple "polyps" *associated* with gastric cancer in 26 per cent of autopsied cases, and Lawrence in 18 per cent.

Some of the reports on the frequency of carcinoma *in* "polyps" in histopathologically proved instances follow: State[46]—23 per cent, Miller[33]—35 per cent; in neoplasms stated as adenomas: Cromer[5]—19 per cent, Carey—37 per cent, and McRoberts[31]—80 per cent (serial section histopathologic examinations).

Broders[2] states that macroscopically carcinoma of the stomach may manifest itself in various forms: as an adenoma or adenomatous polyp.

Finally, it was Ewing's opinion[15] that probably most bulky, polypoid and fungating adenocarcinomas of the stomach develop from such preliminary lesions.

FINANCIAL CONSIDERATIONS

The total cost of a single one of our Schmidt-Helm camera photofluorographic examinations* was $1.46. The total cost of uncovering each silent gastric neoplasm† was $1,068.00. The cost to find each intra-abdominal malignant neoplasm was $2,938.00 and the cost for each gastric malignant neoplasm† was $3,915.00.

We do not feel that these figures represent those that would be obtained in a practical situation. It must be borne in mind that this was an experimental study and experimental costs will run high.

Significant considerations in this light are several in number.

The largest single factor was that 54.5 per cent of the examinees were under the age of fifty (in whom but 4.6 per cent of all gastric cancers occur); that 28.7 per cent were under forty-five (in whom but 2.3 per cent of gastric cancers occur); and that the ratio of the female to male population was 2.7 to 1, whereas cancer of the stomach occurs in but 1 female to each 2 males. Where a survey is done in which the sex and age distribution is equivalent to that of the national population and where the lower age limit is increased even to age forty-five, it can be anticipated that the cost per case would not be above $2,500.00, including the professional fees for interpretation of the miniature films. In practice, the costs for the standard examinations recommended can be excluded from being charged against a survey unit since they would be borne by the examinee in most cases.

Another situation contributing to increased costs was that the survey unit rarely ran at over 50 per cent of its capacity, and therefore the rate of depreciation of nonexpendable materials was almost proportionately increased.

A third factor was that, in our present opinion, at least, periodic resurvey examinations were done at unnecessarily frequent intervals, the greatest majority after periods of one-half year and one year.

Fourth, the roentgenographic equipment used was standard equipment. Some companies responding to requests for information concerning the costs of stripped units have indicated that substantial reductions (about 15–20 per cent) can be anticipated.

Fifth, the Schmidt-Helm camera is an imported one. Information obtained on this point indicates that a camera with a comparable optical system and speed will be manufactured in this country at a slightly lower price.

A sixth factor is that we have included in expense accounting the cost of the conventional studies. Since this was part of the experimental study, no charge was made.

A large item in cost is that from rental of space. Although there was no real monetary expenditure in our study, it is included so that a better general picture would be presented. It is nevertheless conceivable that many survey units might operate in rent-free space, just as ours does.

Lastly, when considering these costs for uncovering a single gastric carcinoma, one must not lose sight of the fact that while discovering this one cancer there have been uncovered an average of three other gastric neoplasms, each adenomatous polyp carrying a fairly high probability of being or becoming malignant.

Against these modifying factors one must balance the professional fees that must be anticipated for the interpretation of the photofluorograms. Estimates on this are based on discussions with radiologists and by considering

* Twenty-one different categories of expendable materials and running costs are included as well as rent, the latter based on $3.00 per sq. ft. per year. Capital equipment is considered on a ten year amortization period. Several items considered on the ten year basis have an anticipated useful life which is longer.

† This includes the basic cost of conventional upper gastrointestinal studies (314) done on the examinees.

the professional charges now being made in North Carolina, where a study is being done under the jurisdiction of the State Board of Health. A fee of around 50 cents per examination is the amount usually volunteered; $1.00 has been the maximum.

Finally, we have considered cost without contributions from the examinees. There is every reason to believe that a portion of the expense of any organizations supporting these examinations would be liquidated on a voluntary basis by the examinees. A pilot study of this point was made by our unit by asking each individual what he would contribute if he were permitted to do so. The result, though probably highly inaccurate in amounts, indicated that even voluntary examinee support can be expected.

As a final test of practicality, it seems best to compare our expenses with the case-finding costs of other screening or survey methods for the detection of neoplasms, and especially with one that already has been generally accepted. The one worthwhile national study is that for cancer of the uterus.

A screening vaginal cervical smear has been reported by Lombard *et al.*[30] as costing between $1.50 and $5.00. Day[7] has indicated that such a smear costs $3.00, including both technical costs and professional fees, and that were this not done as a part of a general purpose examination the cost would be increased two- or three-fold. Rakoff[37] states that the cost of the smear to the examinee is $2.00. Haynes[20] says that the cost per examination is $2.22 in screening studies, exclusive of professional fees; that the standard community fee in his region is $5.00.

Rakoff has indicated that it costs about $3,000.00 to uncover a uterine cancer. At the Strang Cancer Prevention Clinic,[7] the cost to find a case of cancer, in any site, was $3,182.00 in 1949 (less in prior years) with a general anticipated average of $2,500.00 over a number of years; according to Day this would be higher if the studies were limited to a pure detection program in the "asymptomatic population." Pack[36] has learned of some estimates which in some instances amounted to $10,000.00 per cancer found.

In one industrial survey, the cost per proved cancer was $3,690.00, and the cost to the company per employee was $15.45.[1] In a cancer detection center giving general examinations, Jones and Cameron[23] found that it cost $3,468.00 to uncover each cancer and that the cost per person was $16.20.

It becomes obvious that this photofluorographic method to uncover gastric cancer, even at the *experimental expense rate* compares favorably with those of established cancer clinics and, particularly, that the cost per examinee is less than that for the *smear* for the detection of uterine cancer.

We would like now to project our figures against the costs of the present delayed methods of handling gastric cancer.

Even today, of every 100 patients with gastric cancer, only about 4 will live five years and be considered as having their disease arrested.

Now, using a conservative estimate, there is every reason to believe that at least 40 per cent of examinees found to have silent gastric cancer will live five years. Thinking, then, purely of gastric carcinoma, excluding all incidental value of the photofluorographic examinations, disregarding even the adenomatous precursors of carcinoma found, and using this salvage rate of 40 per cent, it would cost $48,000.00* to survey the necessary number of examinees, do conventional gastric roentgenologic studies on 5 per cent of them to confirm 10 cases, operate on the 10 and save the lives of as few as 4 of them.

Using a present operability rate of 75 per cent for any hypothetical 100 cases of gastric cancer diagnosed by the present approach, using an obviously high rate of 10 per cent for the frequency of the roentgen diagnosis† of gastric cancer in any general group of symptomatic patients aged forty-five or over, we find that in the usual course of events to salvage 4 patients, $100,000.00 is spent.

For the $52,000.00 difference in national income *saved*, another 4 persons with silent gastric malignancy can be salvaged through the use of the photofluorographic survey approach. One can calculate the financial savings on a national scale if this thesis is carried further; and one

* $1,000.00 is used for the cost per patient operated upon following diagnosis. $25.00 is used as the fee for the standard gastrointestinal examination.

† Frequency of roentgen diagnosis of gastric cancer—Kirklin,[25] 2.4 per cent; Hodges,[22] 2.8 per cent; Dwyer,[11] 3 per cent; Rigler,[38] 5 per cent. The rate of 10 per cent was used in the example to be certain that the factor that many persons not in the general gastric cancer age, who do have conventional roentgenologic gastric examinations, is considered. Unpublished data[26] about this age factor indicates that the rate of 10 per cent used would still be high.

also might add the income productivity potential of the far greater numbers of salvaged persons living out a relatively normal life span.

PROFESSIONAL CONSIDERATIONS

It is now apparent that the method is practical for the detection of gastric neoplasms in persons with no complaints or with complaints of such type that they do not arouse a significant suspicion of cancer of the stomach in either the person or his physician; that it is practical in accuracy, practical from the aspect of cost per survey examination; and, from a national expenditure basis, that it is more practical than the present method since it gets the patient to the surgeon at a time when a high percentage of cures will be obtained.

It is practical from two lay points that require discussion. The first is public interest. We find this to be considerable. Inadvertent newspaper publicity provoked thousands of telephone calls and letters for appointments. The Medical Director[21] of the American Cancer Society, Philadelphia Division, states that a large percentage of the participants in the detection program come requesting gastric survey as one of the more attractive features of the total examination.

The second point is that if persons harboring silent tumors refused surgery, or if great numbers were inoperable from the standpoint of other serious disease, then the method could be considered impractical from both financial and professional viewpoints. In the two largest roentgenoscopic surveys, surgery was recommended for 19 persons with neoplasms or lesions that could not be clinically differentiated; all were operable (good "surgical risks") and all permitted the necessary surgery to be carried out without delay. Among the 14 persons in the present study for whom surgery was recommended for neoplasms or lesions considered as neoplasms, 11 permitted surgery, 1 is inoperable because of severe cardiovascular disease, 1 refuses surgery at present but desires to be followed, and in 1, an approach which provoked some confusion caused the examinee to change her mind from her original intention of permitting surgery. Therefore, over 90 per cent of these persons have had surgery. This is in contrast to the failure reported in this field by the Hopkins group with their asymptomatic examinees.

The final question is, "Is it practical as far as its professional *application* is concerned?" The answer to this rests with roentgenologists.

In 1948, in discussing roentgenoscopic methods of detection, Kirklin stated that it was impractical in the following manner: he said there were 42,000,000 persons over the age of forty; and assuming that the roentgenoscopic method would be universally applied and two minutes used for a rapid roentgenoscopic survey, and permitting a roentgenologist to work eight hours steadily every day of the year, including Sundays and holidays, it would require the services of 1,917.6 roentgenologists to survey this great group every three months.

Consider these comments but consider others also. First, the most should be done for the most. Detection of cancer can begin at any age but it would seem preferable in the near future to start examinations on persons aged forty-five and over, rather than at the age of forty. This is not an arbitrary choice; it excludes only 2.3 per cent of the gastric cancers, while it excludes 71.6 per cent of the population. This means that there are 42,766,000 persons to survey (1950 census). Derivation from statistics[8,55] indicates that at the present time about 1,000,000 persons aged forty-five or over are now having regular gastrointestinal roentgen examinations done each year. Evidence is being presented that the silent period for some gastric cancers can be as long as two years.[16,54] Obviously, there is a phase where the cancer cannot be seen roentgenologically, and a phase where, although silent, it can have metastasized. It would seem that a reasonable period of time between studies should be two years. (If the ultimate trend shows this to be either too long an interval or too short a

one, it can be revised.) Consequently, it would be necessary to survey a maximum of 20 million persons each year.

There are now 3,000 certified radiologists practicing in this country. If but two-thirds would cooperate in a national effort, it would take thirty to forty minutes each day for just five days a week by each roentgenologist to survey the population over forty-five years of age every two years (10,000 miniature film examinations a year).

It is also recognized that many persons will not be reached, either because of inaccessibility or their disregard for health problems. Most probably a good part of the rural population will be in this group as well as many of the 7,262,000 persons seventy years of age and over, who may not be interested.

Were age fifty used as the lower limit for one of the criteria of selecting suitable candidates, 4.6 per cent of gastric cancers would be excluded, at the same time that 77.8 per cent of the population was excluded. In this instance, each of the 2,000 roentgenologists considered above would need interpret but 8,000 studies each year.

Although this would reduce the number of studies to be interpreted each year, it would not materially affect the amount of time each roentgenologist would spend on them. It *would not affect the cost per miniature film survey*, although it would reduce the cost per proved case of cancer.

Nevertheless, a minimum age of forty-five seems preferable to us, not basically for finding the 2.3 per cent more cancers alone, but to escape excluding many polypoid cancer precursors. Practically, also, it happens that the number of persons in this group is not materially larger than the total number of persons seventy and over. Although the latter should not be excluded, and even though a larger portion might be interested than anticipated, concurrent disease and the short anticipated life span would make surveys of them less rewarding. Therefore, the inclusion of the 8,990,000 persons in this lowest five year group over a two year period is not as prohibitive as the number by itself might imply.

Since conventional gastric examinations will be ordered for about 5 per cent of the examinees having the photofluorographic studies, will this increased load be practical for us to do? Since this number is approximately 1 million studies on persons without significant complaints a year, it would average just slightly over one more roentgenoscopic examination for every certified roentgenologist each day, were all of the 20,000,000 persons surveyed. No appreciable change would occur in the number of conventional studies ordered, as now, on symptomatic patients.

If we accept this problem in its national scope, it will be the first instance in which any single specialty group has undertaken such a productive program for the public good in diagnostic medicine; and it must be taken on a national scale because, even if the present ideal of making every physician's office into a cancer detection center were to materialize, visceral cancers will not be uncovered.

It is almost axiomatic that there can be no appreciable change made in the over-all picture of cancer disaster, until the mortality rate from gastric cancer is materially reduced, since it is the major cause of cancer deaths.

SUMMARY

1. The need for a method for use in the early detection of gastric neoplasm is not debatable.

2. Previous roentgenoscopic detection methods, and other evidence, have indicated that the survival rate for persons who had concealed gastric cancer far exceeds that for symptomatic patients.

3. This experiment in the photofluorographic method for the detection of unsuspected gastric neoplasms establishes the facts that the approach is simple, well received by the laity, safe, accurate, suitable for large population groups, nonrestrictive, inexpensive, capable of uncovering unsuspected gastric cancer and at least one of its

precursors at a more favorable period for surgical treatment, and is professionally practical.

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We are indebted in this work to many persons. Dr. John T. Eads has assisted us by following clinically several of those examinees who have had gastric abnormalities but in whom one could not readily exclude neoplasms as the cause on a roentgenologic basis alone. Mrs. Katherine Goodman, R. T., is primarily responsible for the excellent photofluorographic exposures, the good follow-up response, and the painstaking collection of some of the statistical data. We are indebted to Miss Margaret J. McGann, R. T., for general technical supervision, and to our senior resident staff for professional assistance. We wish to thank the many physicians who have permitted us to use some of their still unpublished data, and officials of the American Cancer Society for their kind assistance.

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DISCUSSION

DR. ROBERT SLOAN, Baltimore, Maryland. In January, 1948, a project was started at The Johns Hopkins Hospital in which routine photofluorographic gastrointestinal studies were performed on all new dispensary patients forty years of age or above. To date, approximately 17,000 such examinations have been performed, and a report on the first 10,000 studies is now in print.

In general, our findings have been in fairly close agreement with those presented today by Drs. Wigh and Swenson. The photofluorographic method does seem to be reasonably accurate as a survey method for evaluating the status of the stomach. There is a low false negative error, but a considerably higher false positive error. The distal antrum is the area most difficult to accurately evaluate on the miniature study, and prepyloric spasm or incomplete filling accounts for a considerable percentage of the false positive errors.

We are not quite as enthusiastic as are the present authors concerning the potentialities of the method as a means of reducing the distressing mortality and morbidity from gastric malignancy. In our own series of cases, we have been able to do relatively little along these lines. One factor has been our difficulty in convincing those individuals with asymptomatic gastric lesions that they should enter the hospital and submit to an exploratory laparotomy. Chance may have given us a poor selection of cases in this regard, but this problem will probably be present to varying degrees in any such series. In a few of our asymptomatic cases with suspected malignancy or its precursor there were other disease processes present which made the risk of exploratory laparotomy seem unduly great. The point is that while earlier diagnosis is essential for reducing the death rate from gastric malignancy with present known methods of therapy, the detection of the lesion is in itself not enough. Almost all of our patients with symptomatic gastric lesions were willing to submit to surgery but, as one would expect, most of these individuals were already beyond hope of cure by that time.

There are certain practical problems involved in attempting to survey large segments of the population above the age of forty. While the technique is relatively simple, the examination is somewhat more laborious and time consuming than is a photofluorographic chest study, and checking suspicious cases with a regular gastrointestinal series is not always a simple procedure. The question also arises as to how frequently the survey should be repeated for any given population group.

We do feel that the method has value in large

institutions where it can be utilized not only for cancer detection, but also as a means of screening the stomach and duodenum in patients with borderline gastrointestinal symptoms. With the photofluorographic technique, a considerable proportion of the normals can be weeded out, thus reducing the number of regular gastrointestinal studies which are necessary.

Dr. Wigh (closing). I want to thank Dr. Sloan for summarizing the work done at The Johns Hopkins Hospital. His group has been very kind to us and has let us have a copy of their unpublished paper. It has been very useful. However, I want to point out that we do not know what portion of the 10,000 persons examined was in an asymptomatic category. Therefore we could not make any precise comment about the incidence of silent neoplasms they uncovered. Also, we continue to feel that there should be no particular difficulty in convincing the majority of people with neoplasms of the stomach to have surgery.

Our opinion is that, as demonstrated, photofluorography is practical. Many of you have indicated at our scientific exhibit that you would cooperate in a wide-scale effort.

We know that we are not going to find every gastric cancer or obtain a five year survival period for each one found. We realize that for some people two years is going to be too long a period for interval study, but it seems to be a good starting point.

We talked about the practicability on a national scale because that is the true objective, and it seemed necessary to compare this work with Dr. Kirklin's statements in 1948. Concerning the 20,000,000 surveys each year, this is the maximum on the two year interval level. I think everyone recognizes that persons seventy years old who have a great many difficulties anyway are not going to be interested in an examination of their asymptomatic stomachs.

The collected figures show that high survival rates will be obtained with silent cancers. Our own follow-up periods are too short to include. I cannot give you Dr. State's figures today, but I do know that for the 14 asymptomatic persons the survival times exceed that which would be anticipated for asymptomatic cases.*

We feel that we are on firm ground in the prediction that at least 40 per cent of persons with silent gastric cancer found by this photofluorographic screening method will live five years and that the detection of the adenomatous precursors will produce a significant reduction in the number of gastric cancers.

* Since this presentation, Dr. State's figures have become available and are now incorporated in the introductory portion of the paper discussing the three year and five year survivors.

MECKEL'S DIVERTICULUM

A NEW ROENTGEN DIAGNOSTIC SIGN AND CASE REPORT

By HENRY H. LERNER, M.D., SAMUEL S. LEVINSON, M.D., *and* A. EUGENE KATEMAN, M.D.

BOSTON, MASSACHUSETTS

A SINGLE case of Meckel's diverticulum, diagnosed roentgenologically, does not ordinarily warrant reporting in the literature. Nearly all radiologists have had the experience of demonstrating this type of diverticulum during the course of a gastrointestinal series.

In this particular case, a new sign which may be useful in diagnosing diverticula of the intestine was noted. It was seen on the

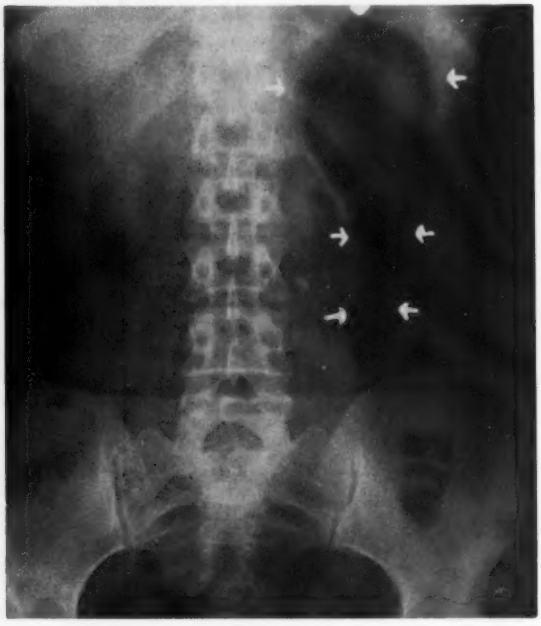

FIG. 1

survey roentgenogram of the abdomen taken prior to the gastrointestinal series. We have been able to make a tentative diagnosis of diverticula on the basis of this evidence in 2 other instances. The diagnostic sign is the visualization of the air-outlined diverticulum on the survey roentgenogram of the abdomen. In one case a Meckel's diverticulum was completely visualized including its neck leading to a segment of small intestine (Fig. 1). In a second case the air-filled sacs of three large jejunal diverticula were visible on the film. In both cases the diverticula were filled with barium during the gastrointestinal roentgen examination and proved by follow-up surgery. In a third case, a large duodenal diverticulum was seen on the survey roentgenogram and proved by filling with barium but was not operated on.

HISTORICAL

The history of Meckel's diverticulum is well known. It has been a recognized entity since 1589. The name of Meckel was attached to it following his description in 1809. It is present in about 2 per cent of normal individuals. By definition, it projects from the free border of the intestine, has a complete intestinal wall, is conical in shape and has a wide mouth. It occurs from 3 cm. to 1 meter above the ileocecal valve. Diverticula not conforming to the above are not called meckelian.

CLASSIFICATION OF DIVERTICULA (Edwards)[1]

(A) *Congenital Diverticula*
  1. Meckel
  2. Non-meckelian
    (a) Giant diverticula
    (b) Diverticula associated with ectopic pancreatic nodules
    (c) Cyst-like diverticula

(B) *Acquired Diverticula*
  1. Primary or hernial type
  2. Secondary
    (a) Diverticula due to disease of the intestinal wall, *e.g.*, ulcer diverticulum of the duodenum
    (b) Traction diverticula
  3. Pseudodiverticula

A. *Congenital Diverticula*
  1. *Meckel's*
    (a) A congenital diverticulum was defined by Meckel as "one identical in

structure with the intestine from which it arises, and consisting therefore of the four coats, mucosa, submucosa, muscularis and serosa."

2. *Non-meckelian*
   (a) *Giant Diverticula.* These are probably duplications of the intestine similar in origin to the paired segments of intestine found in both man and lower animals.
   (b) *Diverticula Associated with Ectopic Pancreas.* These were first described by Zenker in 1861 and are considered to be traction diverticula in that the intestinal wall is drawn up by a mass of aberrant pancreatic tissue.
   (c) *Cyst-like Diverticula.* These are probably due to congenital pouching of the alimentary wall and may be multiple. The lumen between them and the intestine may become sealed off to form true cysts.

B. *Acquired Diverticula* (not concerned with in this report).

CLINICAL SYNDROMES

The normal Meckel's diverticulum does not cause symptoms. When the following abnormalities occur they may become clinically significant: (1) early obliteration of the omphalomesenteric attachment; (2) ectopic epithelium; (3) failure of normal innervation.

(1) The chief result of failure of obliteration of the vitelline veins is attachment of the fundus of the diverticulum to the abdominal wall or possibly development of a cyst in the incompletely obliterated duct.

(2) Pancreatic or gastric epithelium, or both, may occur. Gastric mucosa may be congregated producing a small tumor. More usually it lines the diverticulum, resting on top of a normal small intestinal type of epithelium. Pancreatic epithelium always forms a small tumor mass near the fundus of the diverticulum. The presence of this tumor mass should make one suspect a pancreatic arrest. It might be demonstrable as a filling defect in the air or barium-filled diverticulum and lead to a finer pathological diagnosis by the radiologist.

Both the gastric and pancreatic ectopic epithelium will continue to secrete normal juices. Pancreatic secretion, which is alkaline, is harmless, but the ileal mucous membrane is extremely sensitive to the highly acid juice secreted by the gastric mucosa. Thus, the formation of a chronic peptic ulcer is possible, usually at the junction of the gastric and normal intestinal epithelium, like a jejunal ulcer in a gastroenterostomy. If the gastric mucosa completely lines the Meckel's diverticulum, the ulcer is usually found on the ileal margin of the mouth of the diverticulum. If not, it may occur in the pouch itself. This ulcer behaves just like other peptic ulcers and may bleed, perforate or give rise to pain relieved by food.

(3) Disturbances of motility as evidenced by vague abdominal distress or cramp-like pains in patients with diverticula are probably associated with abnormal innervation. This occurs in many cases when absence of peristalsis produces delay in emptying of the diverticulum.

The occurrence of these complications has been reported from the age of five hours to seventy-seven years. About 45 per cent occur under the age of two and they are twice as common in males as in females. Heterotopic tissue occurs in 16 to 30 per cent of cases.

ROENTGEN DIAGNOSIS

Meckel's diverticula have been demonstrated roentgenologically by several authors.[2,3,5,6,7] No case has been reported where demonstration of the air-filled diverticulum was made on the survey roentgenogram of the abdomen. A correct preoperative diagnosis is rare. In a few cases they have been demonstrated by barium enema. In others, the presence of an abnormal looking loop of small intestine, or a residual pocket of barium in the diverticulum has aroused suspicion leading to the diagnosis.

REPORT OF CASE

The patient was admitted to Bellevue Hospital with a history of an episode of melena accompanied with periumbilical, cramp-like pain

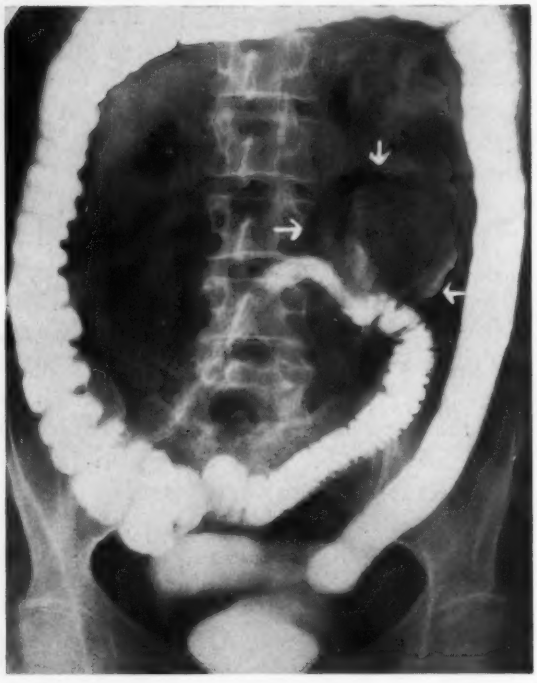

FIG. 2

ten days before admission. A similar episode had occurred three to four years before and at that time melena and red blood were noted. She has had cramp-like, periumbilical pain with bowel movements on occasion for several years. No history consistent with gastric or duodenal ulcer could be obtained. She had become increasingly constipated during the past year.

The physical examination was normal except for tenderness deep in the left lower quadrant.

Roentgen Examination. Survey roentgenogram of the abdomen: There is a large, ovoid, gas-filled shadow in the left upper quadrant which tapers to a funnel shape at its inferior pole. The gas in the stomach can be distinguished from this shadow (Fig. 1). Gastrointestinal series: The esophagus, stomach and duodenum are normal. Barium enema: The colon fills well. The barium spills out readily into the terminal ileum and then into a large diverticulum about 7 inches from the ileocecal valve (Fig. 2). Diagnosis: Meckel's diverticulum.

The patient was then transferred to the Mt. Auburn Hospital for operation by Dr. Samuel S. Levinson.

Operative Note. Under spinal anesthesia a mid right rectus splitting incision was made and the abdomen opened and explored.

A large Meckel's diverticulum was found 7 inches from the ileocecal valve in the terminal ileum, arising from a rather wide base. The diverticulum measured about 4 inches across its base, and about 5 inches from the base to the fundus. The side of the diverticulum was adherent to the mesentery of adjacent small intestine. The adhesions were divided, and the diverticulum together with a short loop of ileum proximal and distal to it was resected between clamps. The ends of the ileum were closed in two layers and a side-to-side anastomosis was done. The mesentery was then closed. The abdomen was otherwise negative.

Pathological Note. The gross specimen (Fig. 3) consists of a previously opened segment of small intestine, measuring 10 cm. in length and having an average diameter of 4 cm. at each line of resection. There is a large previously opened diverticulum, approximately in the middle of the segment, which measures about 8 cm. in length, 7 cm. in width and is about 5 cm. across its base. The surfaces of the segment of small intestine are gray, smooth and glistening. The surfaces near the tip of the diverticulum show areas of dense, grayish-white tissue. Much of the diverticulum is covered with fatty

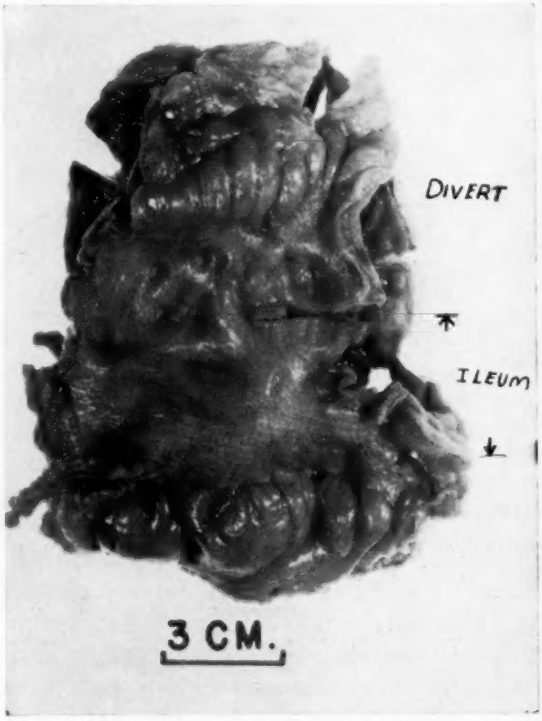

FIG. 3

tissue. The thickness of the wall of the small intestine is slightly greater than that of the diverticulum. The mucosa of the small intestine is in folds. It is grayish-tan after formalin fixation and shows no gross lesions. Some of the mucosa of the diverticulum is lacking in regular folds and is cobbled in appearance; however, the mucosa nearest the intestine has rather regular folds. There is no obvious ulceration of the mucosa.

Diagnosis: Meckel's diverticulum.

Microscopic Findings. The mucosa is everywhere intact and, except for the mucosa covering the blind end, it is everywhere similar to the adjacent small intestinal mucosa. In the blind end, the mucosa has features comparable to that found in the body of the stomach. There is an adequate, but uneven distribution of muscle in the wall of the diverticulum. There is very inadequate and poorly defined sympathetic nerve plexus. Since the motility of the intestine is largely dependent upon an adequate autonomic nervous system, one might expect a lack of peristalsis in the wall of this diverticulum.

DISCUSSION

Since bleeding from the gastrointestinal tract is attributable in over 90 per cent of the cases to a duodenal ulcer, the possibility of a Meckel's diverticulum as the site of the bleeding is rarely considered. Only in children is it thought of in the differential diagnosis.

The practice of taking a survey roentgenogram of the abdomen on all the cases with bleeding from the gastrointestinal tract should be encouraged in the hope of demonstrating an air-filled diverticulum, thus pointing the way to the correct diagnosis. In considering the differential diagnosis of this sign, there are several possibilities. All are rare but should be kept in mind. These are pneumatosis intestinalis,[4] abscess with gas-forming organisms, postoperative accumulations of air (*i.e.*, kidney bed, etc.), or lipoma of the mesentery.

The clinical picture in each condition helps the differentiation and should therefore lead to no difficulty. Filling the diverticulum with barium during the gastrointestinal series confirms the diagnosis.

A history of vague gastrointestinal symptoms in a patient with melena, on whom previous studies have failed to demonstrate a gastric or duodenal ulcer, should arouse suspicion of a Meckel's diverticulum with ulcer.

SUMMARY

A new roentgen sign which may aid in the diagnosis of a Meckel's diverticulum is described. This consists of the air-filled diverticulum being visualized on the survey roentgenogram of the abdomen.

A case of a Meckel's diverticulum diagnosed preoperatively is reported. Three syndromes associated with this anomaly are pointed out.

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DEVELOPMENTAL MALFORMATIONS PRODUCED BY RADIATION

A TIMETABLE OF THEIR DEVELOPMENT*†

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IONIZING radiations have long been known to affect developing and rapidly growing tissues, and increasing interest has centered on the mechanisms by which they affect one tissue and spare another. It has been generally held that roentgen rays damage embryonic tissue, but recent work in several laboratories has shown that the mammalian embryo as well as other developing forms is not uniformly susceptible. In fact, considerable differences in response to irradiation between two embryonic tissues is often demonstrable, and, more important, the same tissue may change its radiosensitivity strikingly as it develops.

The experimental irradiation of pregnant animals at various stages of embryonic and fetal development has shown that the pattern of malformation that results is governed chiefly by the time of the injury, and less by the intensity of the radiation. This time factor has been most clearly emphasized in the studies of Liane B. Russell,[13,14] who irradiated a large series of pregnant mice at known periods of gestation and plotted in detail the gross morphologic deformities that resulted in the developing young. Specific patterns of malformations of the skeleton, the extremities, head, viscera, etc., showed a remarkably consistent and reproducible relation to the time at which radiation injury occurred. Thus, each pattern had a *critical period* for its formation.

In this laboratory a program of study has been in progress to determine the pathologic and biochemical mechanisms by which radiation and other agents alter growth to bring about malformations and the factors that determine the critical periods.[5,6,7] Emphasis has been laid on the nervous system, but the problems of growth and development as a whole have been the aim of the study. The neuroblast has been found to be the cell, thus far, most susceptible to destruction by ionizing radiations in a number of species; destruction of this building block in considerable numbers by radiation causes a variety of malformations of the brain, the pattern changing with the time of the insult. Accompanying this destructive change is an alteration of skeletal growth and certain other alterations. These are not simply the result of cell destruction, for immediate evidence of injury in the skeletal blastema following irradiation has not often been seen histologically, whereas the damaged neuroblast undergoes rapid necrosis in a few hours.

Why the neuroblast should be so radiosensitive is only a partly answered question. It represents a stage in development of the nerve cell in which growth and differentiation are extremely active. Developmentally the nerve cell passes through four stages: (1) primitive germinal neuroepithelium or neurectoderm, (2) neuroblast, (3) immature neuron, and (4) adult neuron. Only the neuroblast is radiosensitive. Coincidentally there are biochemical changes which include a shift from a relative in-

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dependence of aerobic metabolism of glucose in the embryo to an increasing immediate dependence on glucose and then oxygen, as newborn and adult life are approached. Neurectoderm persists through part of embryo life and neuroblasts continue to differentiate well into neonatal life.

The neuroblast is concerned with the production of nucleic acids and proteins, that is, differentiating growth. It is sensitive not only to radiation but to several agents that inhibit sulfhydryl enzymes, to cortisone, to aminopterin, and to radiomimetic drugs such as triethylene melamine and nitrogen mustard. Present evidence suggests that radiosensitivity here is related to a dependence on a system of sulfhydryl enzymes concerned with rapid growth. Mitotic activity is not the determining factor, for in many situations the neuroblasts are not dividing.

In the rat and the mouse, whose gestations are about three weeks, the embryo as a whole is relatively insensitive to radiation during the first week, and it is only toward the end of this week that definite beginnings of various organ systems commence to form.[2] The nervous system is then in its most primitive state and composed of germinal cells (neurectoderm). Although these cells are multiplying they are relatively insensitive to radiation, as are other cells of the embryo at this stage. On the ninth day in the rat, and about the same time in the mouse, remarkable changes occur. Parts of the embryo develop radiosensitivity, and irradiation on this day produces severe malformations of the head, generally characterized by the term anencephaly. This change in susceptibility to radiation appears to coincide with a new pattern of growth, namely rapid differentiation. In respect to the nervous system it coincides with the appearance of neuroblasts. In regard to the skeletal and other organ anlagen, little information is yet available, but preliminary experiments suggest that the mesenchyme and the skeletal blastema may be passing through a developmental stage analogous to the neuroblast, for necrosis of such cells has sometimes been seen after irradiation. During the ninth and early part of the tenth day not only the brain but the head and face are undergoing a rapid developmental transformation in which not only neuroblasts are involved but mesenchymal (soft parts and skeleton), and ectodermal (eye and skin) tissues are also implicated.[3,4,9,10,12] Irradiation in this period causes maldevelopment, or actual failure of development of the derivatives of these elements.

The growth and maturation of organ systems of the developing rat is not a uniform progression (Fig. 1). Transition to the early blastodermic vesicle form occurs on the fifth day and implantation in a decidual crypt is observed on the seventh day (Huber[9]). From then until the ninth day the embryo proper begins to form, and it is on the ninth day that differential growth of embryonic layers into organs and tissues really begins. During the ninth and tenth day several organ systems attain a considerable degree of development toward the ultimate adult form, and in the forty-eight hour period between nine and one-half and eleven and one-half days after insemination twenty somites develop. The heart differentiates from little more than a tube to something substantially resembling a heart in less than three days. Not so in the nervous system and the skeleton. Their differentiation to the adult pattern is spread over a longer period, especially the nervous system. Masses of neuroblasts continue to proliferate and differentiate as successive parts develop. Even at birth the cerebellum has only recently begun to develop and this large part of the brain develops most of its bulk during the first three weeks of postnatal life.[1] These differential growth rates, coupled with the biochemical changes accompanying this cellular development, are what determine the critical periods of the great variety of malformation patterns that can be caused by radiation and other agents.

Experimental irradiation of pregnant

rats, chiefly, and some mice has been carried out, therefore, to determine what patterns of malformation develop when radiation is administered on any given day of gestation. Several dose levels have been used, and irradiation of young animals in the neonatal period has also been done. It is the purpose of this report to give in some detail the results obtained thus far by this program, giving special attention to the nervous system whose malformations are usually the most serious even though they may not be obvious on casual external examination. There are still gaps in the detail of the sequence, especially in the fast changing nine to ten day period where a few hours may make differences in the detail of the pattern of malformative growth. Other questions regarding the possible general effects on over-all embryonic growth in the six to eight day period as well as later are still to be answered. Upon the data presently available a fairly comprehensive timetable can be constructed on which the major deformities of the nervous system can be plotted (Fig. 14).

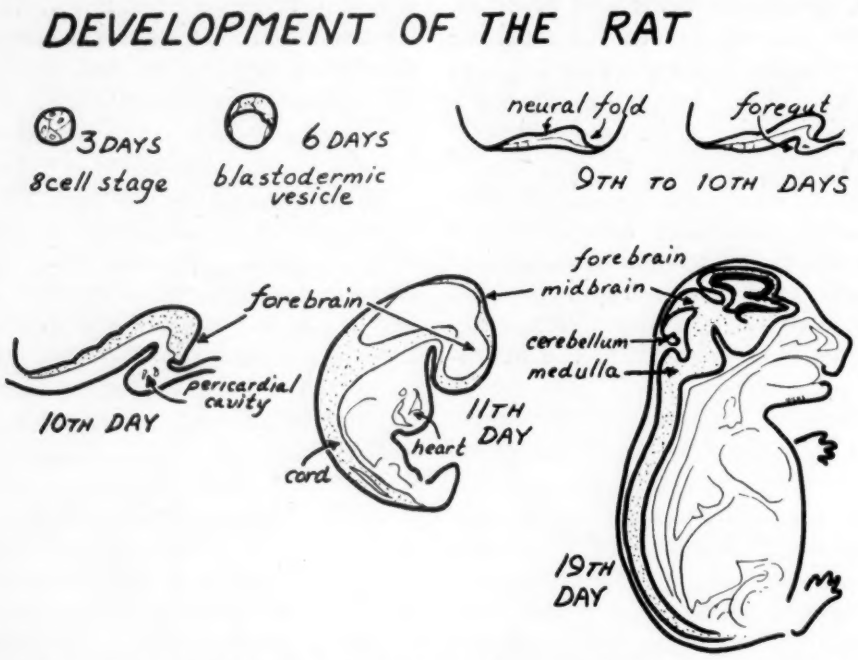

FIG. 1. Schematic representation of several stages of the development of the rat in utero. (Based on Adelman, Butcher, Nicholas, and our own material.)

MATERIALS AND METHODS

White rats were chiefly used but some mice of various pure and mixed strains were also irradiated. The rats were an inbred strain obtained from the Harvard University Biological Laboratory originated about twenty years previously from Wistar Institute stock, or an inbred Sloniker strain kept at the New England Deaconess Hospital for about fifteen years were used. Both nulliparous and multiparous, nonlactating females were used for breeding.

Irradiation was carried out with General Electric Maximar therapy units. The factors were 200 kv., 10 ma., 3 mm. inherent Al filter, target distance 50 cm., about 50 r per minute. The animals were confined in cardboard boxes, or plastic cages with screen tops during exposure. The whole pregnant animal was exposed. The amount of radiation was measured, in air, in these containers with a Victoreen apparatus and corrections made for the container, screen, and backscatter. More than one dose level was used for each gestation day studied. From 100 to 400 r was the useful working range. The apparent dose delivered to the animal, as measured in air, will be the one given throughout the text. Exactly what gets to the fetus in utero has not been estimated.

The duration of gestation was estimated most accurately from the time of copulation. Females for breeding were placed with males daily and each morning their vaginal contents examined for spermatozoa. Appearance of sperm was counted as the beginning of gestation. In other instances, counting was arbitrarily backward from the date of birth, as twenty-two days in rats and twenty-one days in mice.

There are two prime limitations in these experiments. The first is the measurement of radiation, the second is the timing of gestation. Radiation variables were limited by checking the therapy unit at frequent intervals with the Victoreen apparatus, by cross checking a considerable number of animal radiation experiments using the same units and by studying other radiosensitive tissues such as lymphoid tissue, subependymal cells, and gut epithelium in the mother animal and fetal brains in a variety of collateral experiments. Altogether these procedures indicated that the orders of magnitude of the doses stated are usually accurate. The nature of the experiments is such that the time is a more critical factor than the dose within the effective range. Of all the agents used to damage embryos, moreover, ionizing radiation has produced the most uniform selective destruction of cells within a given litter.

The second limiting factor, gestation, is harder to regulate. Rats and mice pair mostly at night but breeding throughout the twenty-four hours is seen frequently in this colony, when permitted. Even when coitus is observed, the exact time of fertilization is unknown, especially since coitus may occur at frequent intervals for an hour or more. In rats, pregnancy may be twenty-one to twenty-three days normally, and in mice twenty or twenty-one days. Suckling of a previous litter at the time of insemination, and other factors may sometimes extend it to well over four weeks. Fertilization and implantation are variable in time, so that slight differences even in the same litter occur. Embryologists find, for these reasons, that in normal studies, development of somites may be a better chronologic scale than days and hours.[2,3,4,9,10,12] The experimental embryologist, unless his procedure calls for direct examination of the embryo or fetus, can never know exactly the gestational time. However, in these experiments the use of several animals for each period, examination of all the young in the litter by various methods, and comparison of results with the results of other laboratories and with normal embryos limits the time error considerably. Also, the present classification of deformities goes by whole days and describes a *sequence* of general patterns. Future experiments, especially those on the ninth day, aimed at exact developmental correlations, will be more greatly hampered by the time element.

The occurrence of spontaneous malformations in inbred strains has virtually no bearing on the present experiments, as the full blown character, the progressive pattern, and the reproducibility of the malformations will show. In other experiments they would be of great importance, for example, where subtle effects of threshold doses were being weighed against spontaneously occurring deformities.

Altogether for these timetable studies, litters from 71 accurately timed rats were used. In addition 14 rats and 21 mice whose gestation time, when radiation was given, was approximately known also contributed to the continuity of the timetable, especially its latter phases. Information regarding the degree and distribution of acute neuroblastic damage was derived from other experiments on several hundred fetuses and newborn animals. For the timetable, the rats were irradiated and allowed to go to term, or in some cases (nine day anencephaly, for example) the young were removed before birth in order to prevent the mother from eating them in whole or in part. Usually, offspring were studied pathologically at intervals of from one day old to a year and a half. The chief tool was histologic examination, serial sections of the head and intermittent or serial sections of the body being made. Fixation was usually in Bouin's fluid or 10 per cent formalin, embedding in paraffin, staining with hematoxylin and eosin, and other stains. From each fetal or newborn litter, cleared skeletal specimens were also prepared, by clearing in alkali and glycerin and staining the young skeleton with alizarin. Others were grossly dissected. From some animals grown to adulthood, roentgenograms of the skeleton were obtained. Only superficial observations were made of the neurologic behavior and breeding patterns of grown animals.

The effects of radiation on the mothers and on the placentas were observed. Four hundred roentgens was the top dose used for timetable studies. Rarely rats given this dose, or even 300 r, died by the end of gestation, or soon after. The small intestine, lymphoid and gonadal tissue began to show some damage between 100 and 200 r,[8] and marrow damage sufficient meas-

urably to affect circulating red and white cells can also develop in this range. Despite these, there was no evidence that the embryo or fetus was materially affected by the maternal reactions. Developmental changes seem to be direct effects of irradiation. In support of this was the delivery of normal litters by mothers receiving 300 to 400 r during the first week of gestation, during which time the embryo is relatively radioresistant. Placental damage was not seen except in one instance where 400 r was given early in pregnancy. At term these placentas showed some microscopic cystic degeneration of the chorionic trophoblastic cell sheets, and the mother had slight residual radiation damage to the intestine and spleen, but the young were normal.

RESULTS

The results can best be presented by a brief over-all survey, then in some detail by days, and finally augmented by illustrations and a timetable (Fig. 14). As stated above, primary attention will be given to the nervous system and other abnormalities will be noted secondarily or where they relate to the nervous system.

General Survey of Results. During the first week, no abnormalities were found in litters that came to term. In some instances, death of the whole litter, possibly from the irradiation, occurred at 400 r. A considerably larger number of animals would be needed to show, however, that this was not due to chance. On the ninth day, there was a dramatic shift to radiosensitivity. Severe malformation or absence of parts of the face, head, eyes, and brain but with relatively normal other structures below the head occurred. This pattern is generally called anencephaly,* but as discussed earlier it represents damage during a rapidly differentiating period for the embryo, and within the litter minor variations are seen. After irradiation on the tenth day, more brain and face succeeded in developing but the nervous part of the eye was still often entirely absent, only an abortive lens and lids forming. In the nine to ten day period, other visceral and skeletal deformities were noted. On the eleventh day, the pattern was characterized by a better developed brain, but there was a narrow aqueduct and a well developed hydrocephalus. The retina and optic nerves were present, but the former was malformed. On the twelfth day, the cerebrum was still malformed, but it was more the intrinsic architecture than the over-all gross development that was affected unless the irradiation was heavy. From the ninth through the twelfth days, diminishing degrees of encephalocele were present, with corresponding deficiencies in the vertex and crown of the skull. No fetuses with these severest defects survived past birth, the mother usually destroying them. In cases where irradiation was carried out after the twelfth day, viability was usual, and a number of animals were allowed to grow to adult life. The brain defects from the thirteenth day on through the eighteenth were characterized by a decreasing degree of over-all microcephaly, architectural disturbances of the cerebral cortex, hippocampus and basal ganglia. In the thirteen to sixteen day period, the anatomic positional relationships of the regions of the striatum, hippocampus and corpus callosum were markedly disfigured. No corpus callosum developed following moderately heavy irradiation from the ninth to eighteenth or nineteenth days, and in frontal sections the striatum appeared displaced upward to be in continuation with the deficient hippocampus and cingular cortex regions. As term was approached, these malformations became less and less gross and more and more a matter of disturbed architecture and a deficiency of cells. Skeletal deformities became less and less.

When neuroblastic zones in the fetus are exposed to radiation, say 150 r, many of the cells die. Those not killed are seemingly unaffected—mitoses are present and normal four hours later, while the necrotic cells continue to disintegrate, and are phagocytosed a few hours later. Neurectoderm, where still present, continues seemingly undisturbed. Within twenty-four to forty-eight hours after irradiation, the

* Anencephaly literally means "no brain," but like the word anemia it is seldom used in the absolute sense. As is usually the case in humans, these animals show varying degrees of the condition.

residual neuroblasts and apparently neurectoderm actively proliferate to form rosettes and what resemble primitive neural canals. These are lined by rapidly multiplying germinal cells (neuroectoderm) and are surrounded by a thick zone of neuroblasts. Depending on their position in the brain or cord and the course of growth in the region in which they develop, they either mature rapidly into nervous tissue or continue as focal sources of neuroblasts for a while. In the cortex or hippocampus, the net result as seen at birth is the formation of a bizarre architectural pattern of neurons and fiber bundles often oriented in discrete or confluent rosettes. All degrees of severity are seen. In the striatum, such foci continue to grow at birth like the periventricular neuroblastic zones normally do, but the result is a bizarre striatum and aberrant ependymal lined cavities ("porencephaly"). The retina throughout fetal life follows a similar basic growth pattern after irradiation; that is, surviving neuroblasts form rosettes which determine the ultimate deficient and malformed adult retina. The retina and spinal cord, however, decrease slightly in radiosensitivity as term approaches, requiring higher doses for damage than the corresponding striatal regions.

The cerebellum does not develop appreciably until near term and accomplishes much of its growth during the first three weeks of postnatal life. During this period its neuroblastic component is vulnerable to irradiation. Prenatal irradiation disturbs the basic shape of the cerebellum (probably as far back as the fifteenth or sixteenth day) while postnatal exposure affects more the intrinsic cellular architecture, especially the formation of the granular cell layers.

The dose of radiation, though a secondary factor in the malformations, is nevertheless important. In the range of 100 to 250 r, it is often difficult to find consistent differences in degrees of destruction. Three hundred or four hundred roentgens may be much more destructive, so that bulk defects may be the chief characters of the malformation.

Below 100 r neuroblastic damage becomes less and less so that at 30 to 40 r relatively few cells in the anterior striatum and its junction with the ventricular angles, where the callosum is or will form, are destroyed. These zones are the most radiosensitive during fetal life. It would probably be impossible to demonstrate abnormalities in these low dose animals later in life, so obscured would they be by development. As is widely known throughout the animal kingdom, a few missing nerve cells are difficult to recognize by their absence. At 400 r destruction is extensive and the young have severe degrees of the characteristic malformation, and gross deficit of brain tissue becomes very notable. In terms of skeletal disorders, the larger the dose, the smaller the young animal may often be, and the more severe the skeletal defects. A degree of runting is frequent, but not constant, in animals irradiated in utero from the ninth day to term in the dose levels 100 to 400 r, and also in animals irradiated the first few postnatal days.

Results in Detail. These are presented in terms of rats whose gestations were for the most part accurately known. Information from approximately known gestations is not specifically mentioned except in a few instances where they were useful as supplementary data.

First week: Irradiation on any day through the seventh day after copulation produced no developmental abnormalities. Twenty-four females were used. In 4, no litters resulted. Whether this was due to an irradiation effect, spontaneous involution, or failure of fertilization cannot be determined.

Eighth day: Six litters were obtained following irradiation of 7 females on the eighth day after copulation. The young were studied at birth or later in life. The litters were all normal.

Ninth day: Rats irradiated on what was counted as the ninth day would, by our method of counting, have been inseminated a little over nine days previously to about nine and three-fourths days. It is toward the end of the ninth day that somites begin to develop and differentiation of the nervous system gets under way. Since the malformation produced depends primarily on the radiosensitiveness of

certain parts of the embryo at a given moment, our experiments on this day seem to have been spotted over the whole nine day interval. Seven rats were irradiated on this day. Doses of 50, 100, 150 roentgens were given in these instances for it seemed likely that the higher doses would add little to what 150 r could do. In one large litter (150 r) all the young showed severe malformation of the head, the remainder of the body being normal (Fig. 2). In this litter, with the skin. Posteriorly, as the occipital level was approached, fairly normal brain stem became evident, so that at the cerebellar-medullary level little malformation was evident except that the medulla showed virtually no longitudinal fiber bundles. Ventrally the "anencephalic" brain mass formed a cavity lined with elongated parallelly arranged immature neural cells, suggestive of the lining of young ependymal cavities and of retina. It formed two ill defined

FIG. 2. Anencephaly in term fetal rats. Irradiation with 150 r on the ninth day of gestation.

minor variations, there was severe interference with the formation of the anterior and dorsal head above the maxilla. The lower jaw and maxilla developed in some instances normally; in others they, too, were incomplete. In the animal from which the illustrations in Figures 3 and 4 are drawn, the lower jaw and maxilla developed, but the head above was a tiny elongated, hodge-podge of its components, abortively formed or absent. Partially to completely enclose in a thin layer of epidermis was an irregular matrix of connective tissue, which in turn held an elongated little "brain." This was partly surrounded by leptomeninges, but elsewhere it was contiguous with the skin and its appendages laterally and dorsally, or below, with a scarcely recognizable base of the skull. This brain was a lobulated mass of irregularly disposed neurons, nerve fibers, sometimes in bundles, and glia—it simply looked like a mass of malformed brain tissue. A few minute islands of such tissue lay between the brain proper and lateral angles, but if these represented the original neural parts of the optic vesicles, the structure as a whole was more cyclopian than bilateral. In this animal the anterior pituitary grew up into the roof of the mouth, but failed to contact the brain. It formed as a mass of epithelial glandular elements, histologically reminiscent of oral mucous membrane appendages or even the cellular pattern of a craniopharyngioma (Fig. 4).

None of these tissues had the characteristics of true neoplasms, as has sometimes been implied. Admittedly it is difficult to define a tumor (neoplasm) in rigid terms, but the growths here are simply the result of removing or changing the growth rates of some of the developing building blocks in a normal embryo. In no instance did these abnormally formed tissues take on progressive and independent growth properties to the extent that they replaced, destroyed, or invaded other components. They all seemed to be heading toward the goal of mature

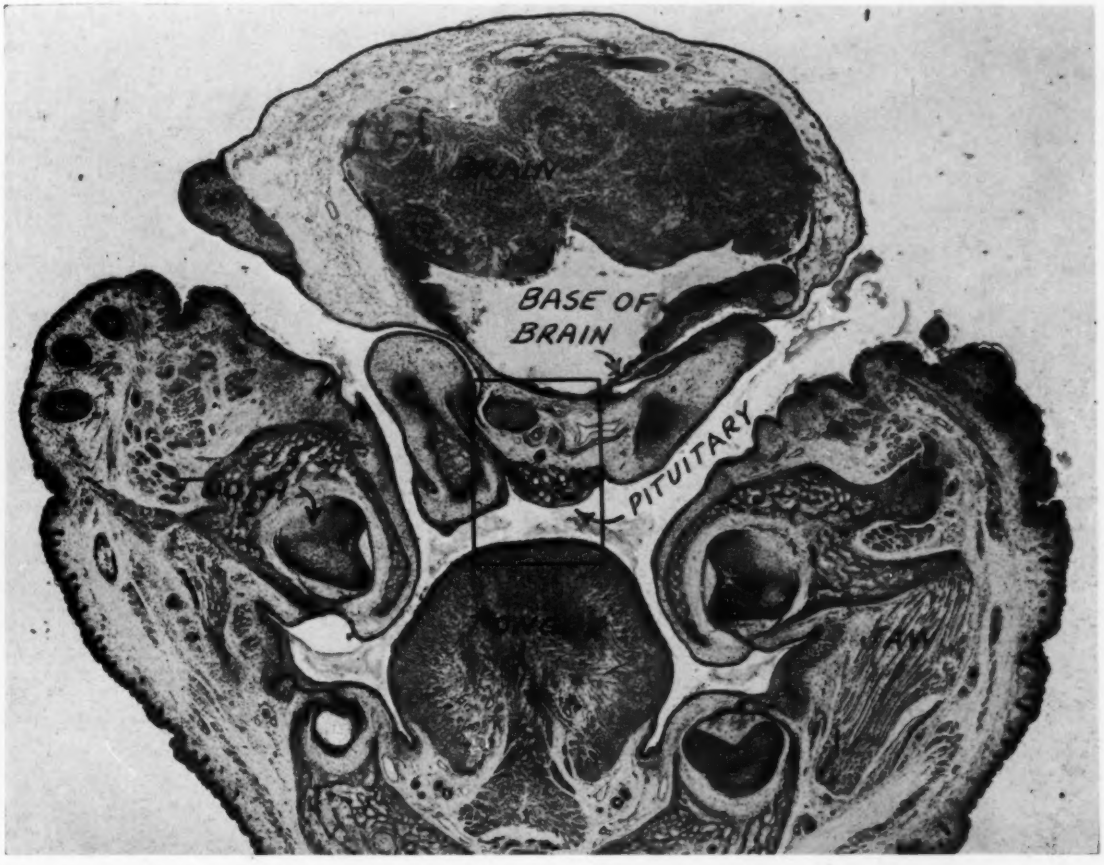

Fig. 3. Anencephaly. Frontal section through the head of a litter mate of those shown in Figure 2. The lower jaw is fairly well formed, but the upper and frontal part of the head is a grotesque caricature composed of abortively formed head structures. Rectangle is shown in Figure 4. (Low power, hematoxylin and eosin.)

organoid differentiation, bizarre as the aggregate result might be in terms of normal anatomy and function. To extend the term neoplasia to embrace every sort of abnormal growth would cloud an already very difficult concept.

In another litter of 3 rats that received 100 r on the ninth day, anencephaly with a slight degree of encephalocele occurred, but in 2 of these the under jaw and distal nose seemed well formed. These 2 had very little of the anterior brain, and an encephalocelic sac or "cranial blister" with a skull defect at the vertex (which the mother ate), and otherwise normal bodies. The occipital skull was elongated and closely approximated the first cervical vertebra. The eyes were incompletely formed both externally and in respect to the retina. In the third member of the litter, the brain was well formed except that the optic nerves and retina did not develop, although the lens, lids, and appendages formed abortively. The olfactory lobes and anterior nasal structures were smaller than normal. It may be judged that this animal was not quite as far along developmentally as his brothers at the moment of irradiation. Probably also this litter was irradiated later on the ninth day than the first litter described above, as judged by the fact that the maxillae as well as other structures in the foreface had already been established at the time of irradiation.[3,4,9,10,12]

In a third litter irradiated on the ninth day, the fetuses were removed on the fifteenth day. They had already become full fledged anencephalics, having a pattern identical with the first litter described and shown in Figures 2 and 3. The whole upper head and sometimes maxillae were distorted.

In three other litters, irradiated on the ninth day, no abnormalities developed. In still another litter, malformation of the retina was the only defect. These findings are attributable to

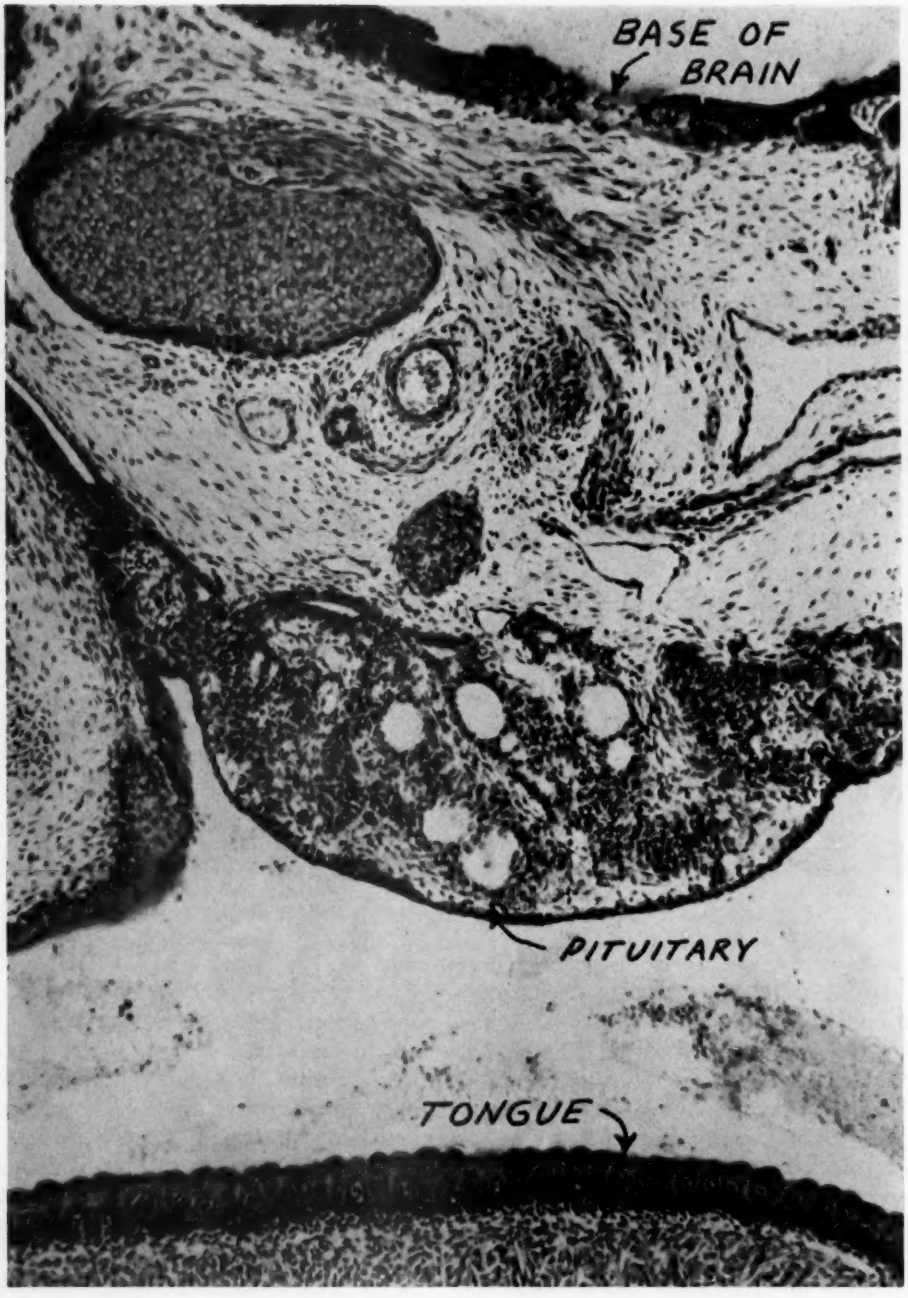

FIG. 4. Anencephaly. A higher power view of the pituitary in Figure 3. Its histologic pattern is reminiscent of appendages of the oral mucosa. (×125, hematoxylin and eosin.)

the time of irradiation, namely, early on the ninth day.

In none of the ninth day litters were visceral or specific skeletal deformities (except the head) found.

Tenth day: Malformations, generally categorized as anencephaly, characterized the results of irradiation on the ninth day. On the basis of normal embryologic observations and their correlation with the ninth day malformations, the radiosensitive period of the ninth day is, in its last few hours, approaching the tenth day. The malformations of the tenth, eleventh, and twelfth days merge into one another fairly smoothly.

After irradiation on the tenth day, severe de-

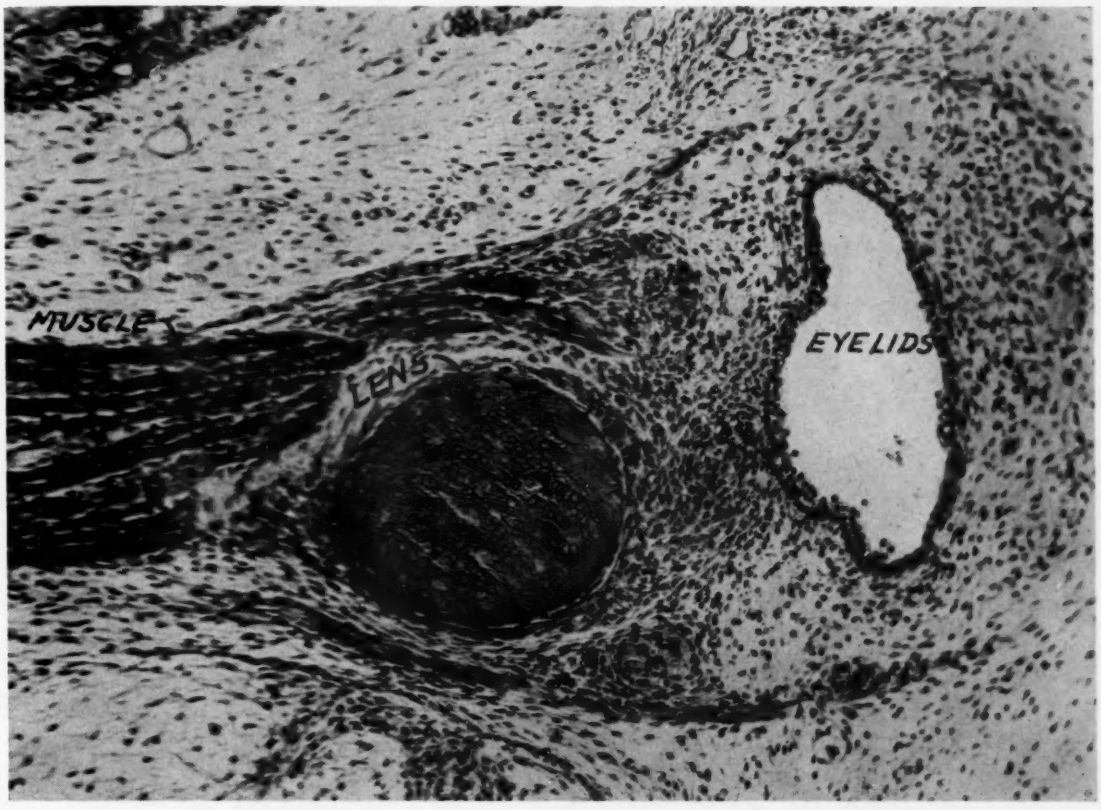

Fig. 5. Malformation of the eye in a newborn rat, following irradiation on the tenth day of gestation. No central nervous parts developed, but lens, lids, muscles, and appendages are represented. (×150, hematoxylin and eosin.)

fects of the forebrain dorsally and anteriorly occurred with a corresponding failure of the vertical portions of the parietal skull bones to develop. There was usually a degree of encephalocele as a result. There was absence of the optic nerves, but the external eye—ectodermal derivatives, lens, lids, appendages—developed, though abortively. In some instances only a scant nidus of a lens was evident, in others there was a fair representation of the extraneural parts of the eye, but no retina or optic nerve (Fig. 5 and 8).

Skeletal deformities also developed. In addition to those of the skull, the whole skeleton was small and the long bones of the extremities disproportionately small in some, but not all, instances. Visceral abnormalities were absent except a dilated renal pelvis in some animals. The lower urogenital tracts were normal.

Eleventh day: Irradiation on the eleventh day of gestation caused two interesting deformities: hydrocephalus and a narrow aqueduct. The two were associated in the four different litters irradiated on this day. There was no intrinsic malformation of the aqueduct per se, other than its small size. Sometimes the ependymal lining cells were closely approximated, in others the duct was open. The part that was narrow was the proximal part of the iter from the third ventricle. The ventricular dilatation particularly affected the lateral ventricles and the third was also dilated. The cortex and underlying white matter of the cerebral hemispheres was thinner than normal (Fig. 6) and the hippocampus, except most laterally and caudally, was virtually unformed. The midbrain architecture was moderately jumbled and its total bulk slightly reduced. Since this hydrocephalus is not conspicuous on other days and is associated with the narrow aqueduct (Fig. 7) a causal relationship seems likely. The deficiency in substance of the hemispheres does not account alone for the dilated ventricles.

In the eleven day animals no corpus callosum formed. The striatum and especially thalamic regions were reduced in bulk, but the exact cellular architectural abnormalities have not been analyzed. The external eyes formed, but were

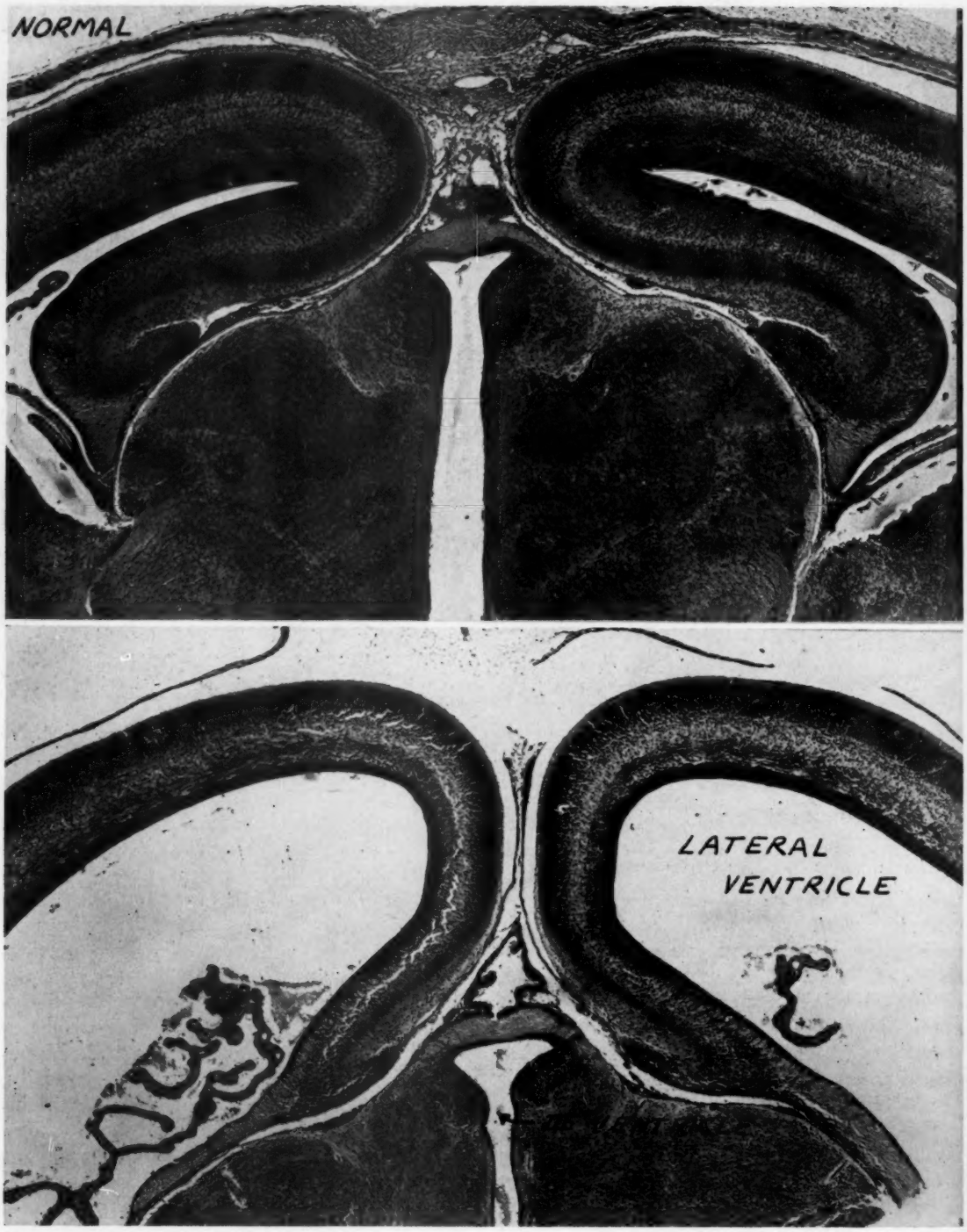

FIG. 6. Hydrocephalus in a newborn rat, the result of 150 r irradiation on the eleventh day of gestation. Normal is shown above. (Low power, hematoxylin and eosin.)

small. The retina was often severely malformed, and in heavier doses the lens was imperfect. In some instances acute hemorrhage separated the retina from the choroid. The retinal abnormalities took the form of neuroblastic rosettes and proliferation of a few new capillaries anteriorly from the region of the head of the optic nerve into the vitreous. The

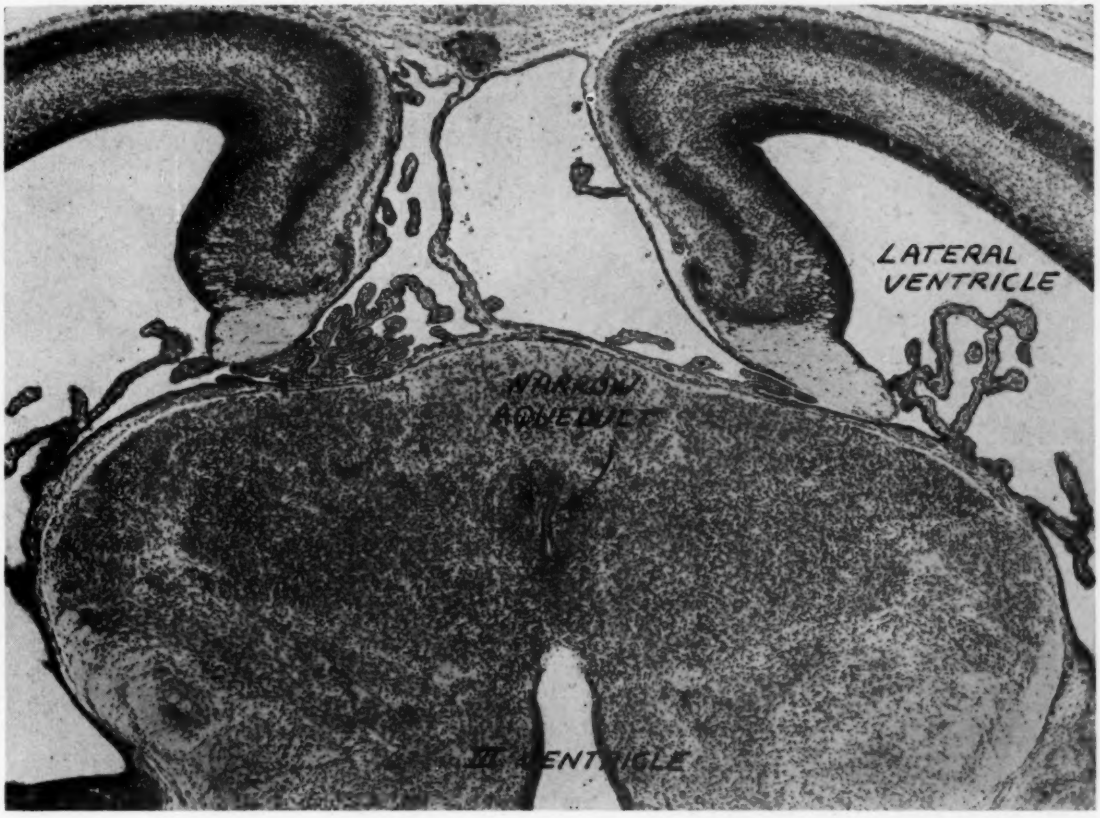

Fig. 7. Narrow aqueduct associated with hydrocephalus. In this experiment 300 r was given on the eleventh day of gestation. (Low power, hematoxylin and eosin.)

picture was not, however, that of retrolental fibroplasia.

Some degree of encephalocele and skull defect involving the posterior vertex was present in some animals at higher dose levels, but did not primarily account for the hydrocephalus. The face and head were shorter than normal. Throughout the period of ten to fourteen days, lighter doses caused abnormal underdevelopment of the cerebral hemispheres, while heavier doses were so destructive that much of the dorsal cerebrum was absent (see illustrations). A smaller than normal skeleton, in addition to the skull defect, was noted. In some animals the elbows were fused, in others the sacral spine was imperfectly formed, though a full blown spina bifida was not recognized. Often the femur was disproportionately short. Visceral malformations were not found.

Twelfth day: The deformities produced by irradiating on the twelfth day are in the brain, skull, and skeleton (Fig. 8 and 9). In one litter given 300 r, a heavy dose, there was some degree of encephalocele at the posterior vertex in 6 of 9 young, involving the posterior cerebral hemispheres. The encephalocele was covered by scalp and an incomplete thin skull. The defect suggested the markedly defective pattern seen in some animals on earlier days, but it was situated more caudally, and the ventral and anterior parts of the brain were better developed. The striatal regions were bizarre and the ventricles themselves irregular in contour. The brain stem was reduced in volume; the dorsal cervical cord showed some jumbling of neurons. Though the ventricles were relatively dilated, the real hydrocephalic pattern of the eleventh day was not present.

The skeleton was small, the toes incompletely formed (a finding more usual on the thirteenth day). Some spinal alterations similar to the eleventh day were occasionally present. The internal ear was irregular in its bony configuration and slightly misplaced ventralward. The heads and snouts were short. The eyes were very small. Microscopically, the retina was almost completely wiped out and the lens showed an irregular cellular architecture.

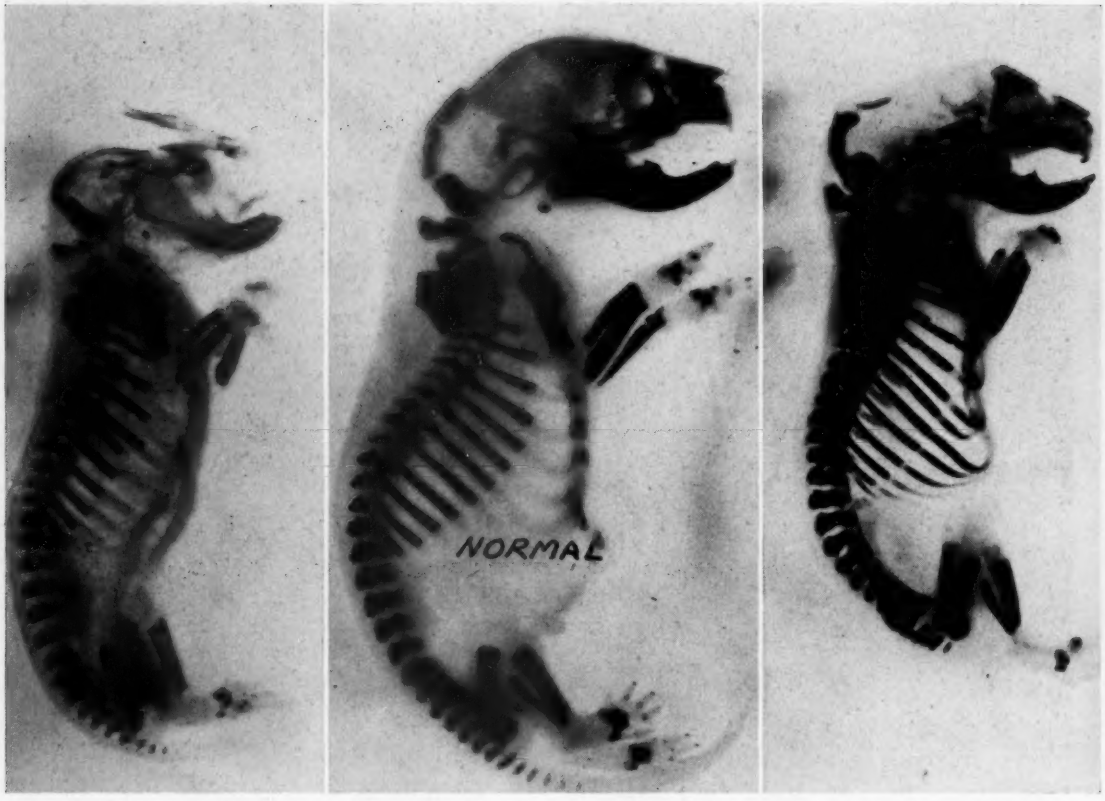

Fig. 8. Effects of irradiation on the twelfth day (right) and tenth day (left). Newborn rats. The center one is normal.

A lighter dose, 150 r, on the twelfth day produced a less destructive effect, with a somewhat milder though equally fantastic distortion of the brain (Fig. 10). The olfactory and frontal cortexes were jumbled and showed some neuron rosettes. The zones dorsal and lateral to the lateral ventricles, and other periventricular regions somewhat less, were largely made up of large rosettes, lined either with ependymal or less differentiated cells and surrounded by a thick radiating zone of neuroblasts and maturing neurons. Some of these rosettes had a sizable cavity occasionally connecting with the main ventricle and would be termed "porencephaly." The hippocampus was virtually absent superiorly and anteriorly, but was present and well developed at the inferior margin of the ventricle. The corpus callosum was absent, the lateral ventricles were slightly dilated. The posterior cerebral mantles showed no jumbling of architecture, but the ependymal cells of the canal in the cervical cord showed possibly more of a rosette pattern than usual.

The damage in these animals in contrast to the 300 r litter was a result of lesser injury to the periventricular and cerebral hemispheric derivatives. The neuroblasts of these zones are the ones most easily damaged, as noted above and in other studies, but more survived here (150 r) to produce more brain tissue.

In two other litters, 200 r was given. In both, the head and feet showed deformities and the pattern was somewhat similar to that after 300 r. In still another litter (150 r) animals were allowed to mature. These had deformities of the spine, feet, neck, short heads, small eyes, severely malformed brains like those described above (150 r). They managed to get along in matters of feeding and with other rats, though they were clumsy and walked with a hopping or waddling gait. When young they played actively, but they were sluggish in later months. Breeding habits (if any) of twelfth day animals were not studied.

Thirteenth day: The newborn from rats irradiated on the thirteenth day of pregnancy showed relatively inconspicuous externally visible deformities. They had defective toes, some-

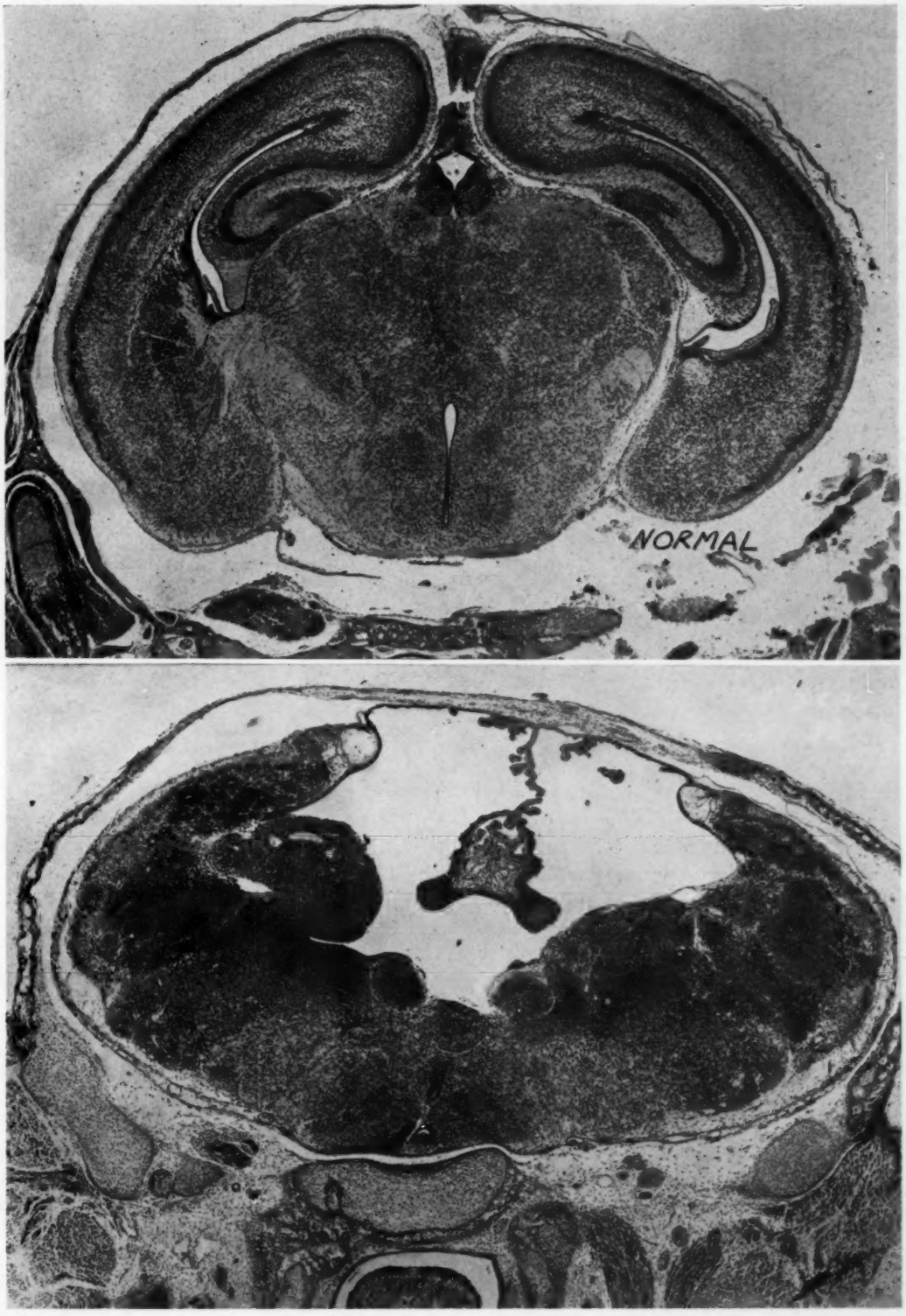

FIG. 9. Malformation of the cerebrum of a newborn rat following heavy irradiation (300 r) on the twelfth day of gestation compared with the normal. Compare with Figure 10. (Low power, hematoxylin and eosin.)

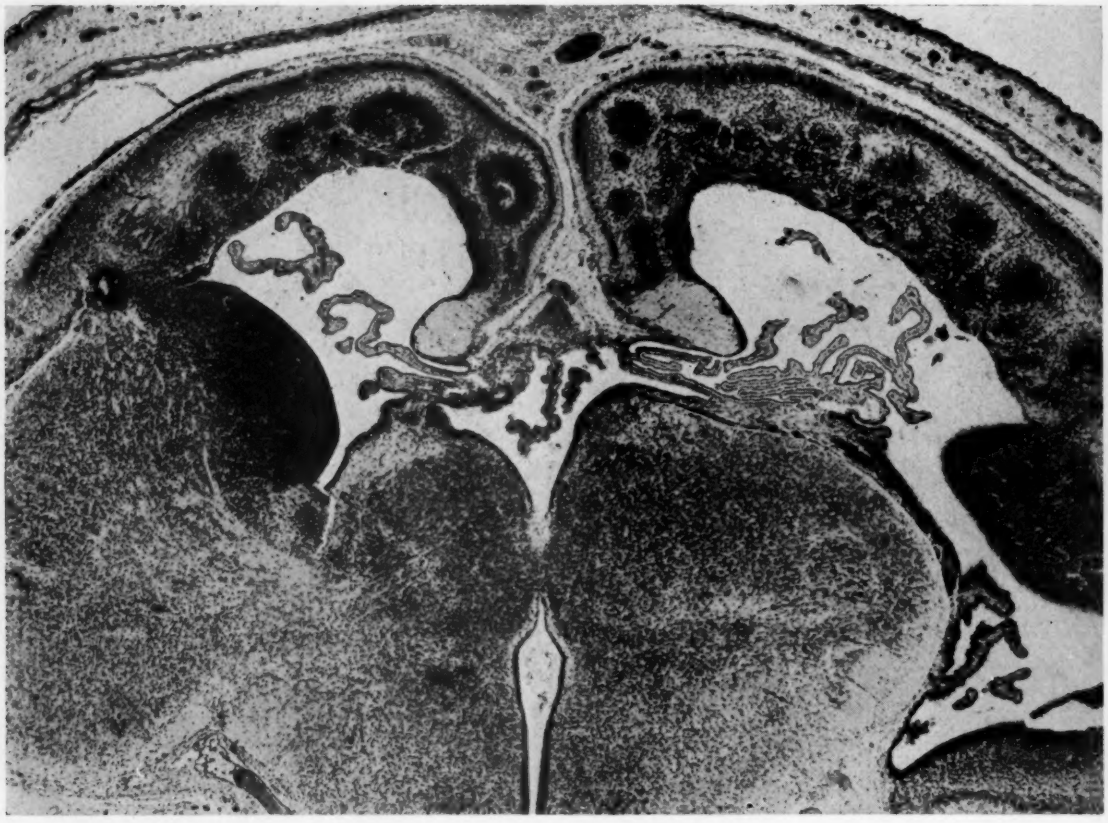

Fig. 10. Malformation of the cerebrum of a newborn rat following 150 r, on the twelfth day of gestation. Compare with Figure 9. In both, the forebrain was being defined at time of irradiation, but in this animal with a lower dose more neuroblasts remained to produce relatively more brain. (Low power, hematoxylin and eosin.)

what small eyes as they grew up, sometimes but not always a small skeleton, shortening of the neck due to narrowing of the vertebrae and sometimes irregularities of the lumbar vertebrae.

The brain defects were largely a matter of severe malformation of the striatum, its junction with the medial cerebral cortex and the hippocampus. These areas, on section, were the site of numerous rosettes and totally jumbled architecture in the newborn, and in mature animals this pattern led to rosettes and jumbled architecture of corresponding neurons and a grossly malformed relationship between the regions. With the corpus callosum absent, the striatum, anterodorsal hippocampal region, and cingular cortex formed a continuum of striatum-like cell masses with some fiber bundles. The appearance, in frontal sections, was of the striatum extending up then medially over the lateral ventricles to fuse with the cingular cortex and take the place of the corpus callosum and hippocampus. Anteriorly the same sort of dorsomedial "displacement" was evident (Fig. 10) to the extent that where the hemispheres should appear as two separate halves in frontal sections they were fused. Here the lateral ventricles were out of place, being relatively more forward and ventral than normal.

With 300 r the type of deformity described was intensified and deficit became marked. The striatal regions and cerebral hemispheres anteriorly were strikingly reduced in bulk and bizarre in architecture. The retina was present, but malformed, and the lens cells irregularly disposed. Proliferation of retinal capillaries occurred as noted on the eleventh day. No optic nerves could be discerned except at the retina. The peduncles and the striatal fiber bundles were virtually absent. Caudally the brain was much less abnormal although the hippocampus was extremely deficient. The pituitary and pineal were unremarkable.

Fourteenth day: Irradiation was carried out on

Fig. 11. Malformation of the brain in a rat irradiated in utero on the sixteenth day of gestation. The disposition of the striatum upward, its bizarre shape, and fusion of the hemispheres medially are notable. (Low power, hematoxylin and eosin.)

two litters, at 200 and 300 roentgens. The malformation involved the dorsal cerebrum, striatum and the eye principally. The pattern was not unlike the thirteenth day, but lateral, ventral and hippocampal portions of the cerebrum were further along in development. The corpus callosum was absent. In the 300 r litter the vertex of the cerebral hemisphere was especially defective and the confluence of third and lateral ventricles enlarged in association with a large choroid plexus. The head was shortened and flat. The lens was irregular in cellular architecture and the retina malformed. The severity of defect was less in the 200 r experiment. Both litters showed slight irregularities in the bases of the cerebellar hemispheres.

Fifteenth day: Two litters, one irradiated at 200 r and one at 300 r were studied. Malformations were largely limited to the striatum, the dorsal cerebral cortical mantle, and the hippocampus. There was minimal abnormality of the anterior olfactory brain. The frontal, dorsal, and dorsolateral cerebral cortex showed a jumbled architecture with patchy clustering of neurons and slight tendency to rosette formation. The lateral ventricles were slightly irregular in outline. The corpus callosum was absent; the hippocampus showed architectural damage like that of the cortex. The striatum was better formed laterally than on foregoing days, but medially was deficient. The thalamus and remaining interbrain was smaller than normal, but architectural details were not analyzed. Slight irregularities of the cerebellar folia were noted grossly. The retinas showed rosettes but the lenses were normal. No general skeletal abnormalities were noted. The mother of the 300 r litter died six days postpartum apparently as a late result of irradiation, as judged from necropsy.

Sixteenth day: Six litters were obtained from rats irradiated on the sixteenth day of pregnancy. The pattern of malformation was similar to that of fifteen days but was more a matter of architectural abnormalities and less of gross derangement of parts, such as was seen in fore-

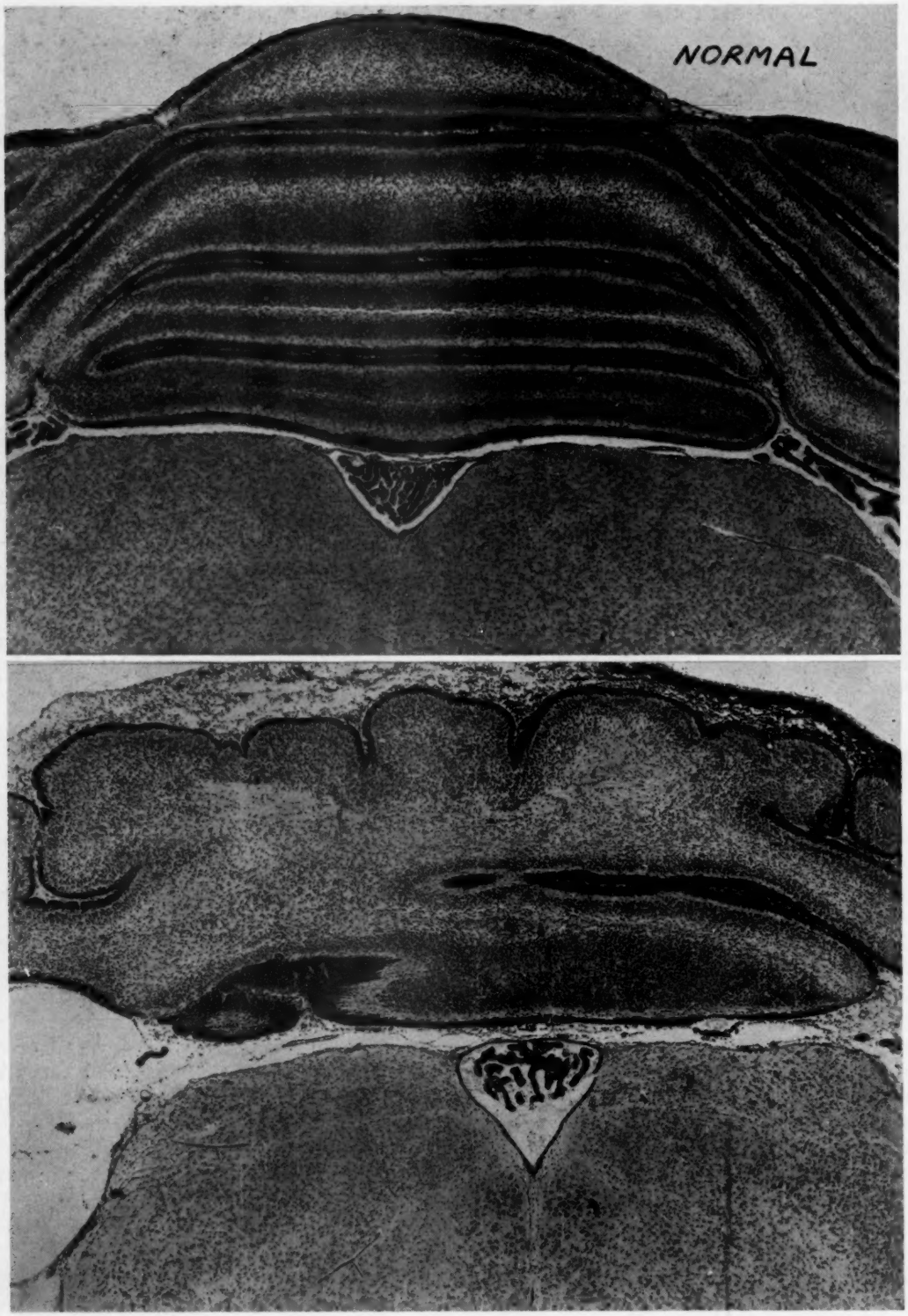

FIG. 12. Early malformation of the cerebellum in a young rat irradiated one day before birth. The folia are coarse and the granule cell layers deficient as compared with the normal. (Low power, hematoxylin and eosin.)

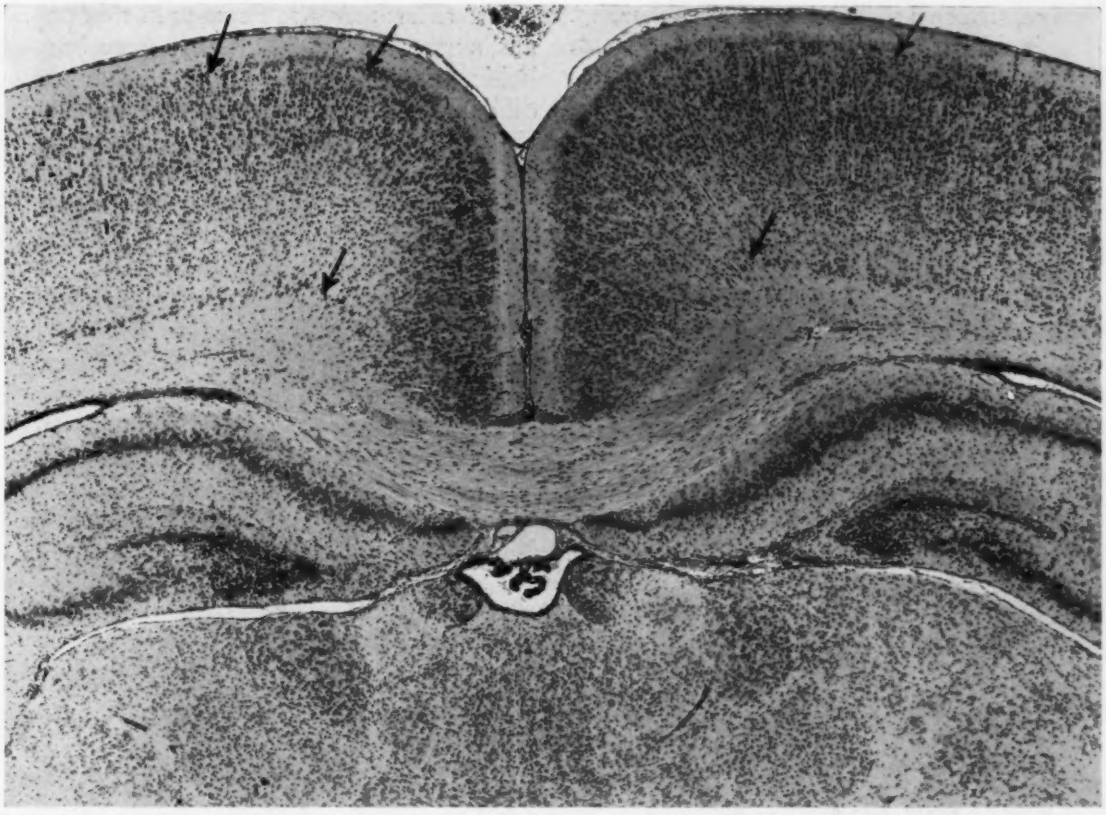

Fig. 13. Malformation of the cerebral cortex, characterized by sparsity and slight clustering of neurons in outer and inner layers (II and VI). This is the same animal represented in Figure 12. (Low power, hematoxylin and eosin.)

going animals in the striatum. The doses here ranged from 100 to 250 r so that the effect of top dosage was not observed (Fig. 11).

Seventeen to twenty-one days: A number of accurately timed pregnant animals was irradiated from 100 to 300 r in this period. Included for supplementary data were some approximately timed and some mice. Through the eighteenth and sometimes up to the nineteenth day of gestation, irradiation prevented formation of the corpus callosum; or sometimes at lower doses it was incompletely developed, appearing only in its anterior portion. As term was approached, more and more evidence of damage to the cerebellum was seen, being reflected chiefly in coarsening of the folia and deficiencies of the granular cell layers. Figure 12 shows the effects of irradiation on the development of the cerebellum in a seven day old rat, irradiated with 200 r in utero on the twentieth day of gestation. Both folial and granule cell defects are seen. As the animal matures, granule cell layers will form from the outer thin, irregular neuroblastic layer still present ("outer granular zone"), but they will be irregular, as litter mates and other animals have shown. Irradiation after birth produces, as would be expected, less disturbance of gross folial configuration and relatively more damage to the granular component.

Cortical and striatal damage toward term and after birth is less dramatic, but nonetheless severe when substantial radiation is given. The striatal effects represent a deficiency in the medial caudate-putamen mass difficult to recognize. More readily recognized are the cortical defects. The cortical defect resulting from irradiation on the twentieth day of gestation is a slight clustering and disturbed polarity of the outermost cell zones (laminae II and III) and considerable numerical lack of the neurons. In lamina VI there is also some deficiency of cells. The hippocampus and interbrain appear undisturbed except the medial striatum as noted and sometimes irregularity of the medial fascia den-

tata cells. Such a picture is shown in Figure 13. This is the forebrain of the same animal shown in Figure 12.

DISCUSSION OF RESULTS

Some general remarks appropriate to the whole study may be made here. First, the study is still largely a descriptive one, aimed at laying out an over-all picture of the *changing* pattern that follows damage to the developing animal in successive periods of its growth. It has seemed advisable to approach the problem first in a broad way, then to work out details later. The advantages of this over the reverse approach is that a general view of the problem is gained first and its overlaps and interrelations are seen more easily.

One of the most interesting phases of this study is the nine and ten day period of gestation (see Fig. 1). So rapidly changing a period is this in terms of differential development that many more studies will be needed to correlate in detail the malformations produced in this interval. If the thesis advanced earlier in this paper and supported by preliminary experiments holds, namely that other, perhaps all, differentially developing tissues pass through a radiosensitive stage analogous to the neuroblast, then deformities of each may be expected to occur. But such sensitivity may not be the only kind that we are dealing with. Skeletal blastema may be radiosensitive at a very early stage, but growing embryonic cartilage may also be. In the dose ranges used here, we have seen no destructive cartilage damage. Acute experiments were, however, conducted where fetuses were studied twenty-four hours after 600 r was given to the mother. The destructive picture in some of these extended beyond a selective action on neuroblasts. Scattered cartilage cells were necrotic and other cells in the mesenchyme and in some other tissues were also. These latter were in excess of the spontaneous necrosis that occurs in varying, but minimal, degrees in the nervous system and other tissues of fetuses throughout in-

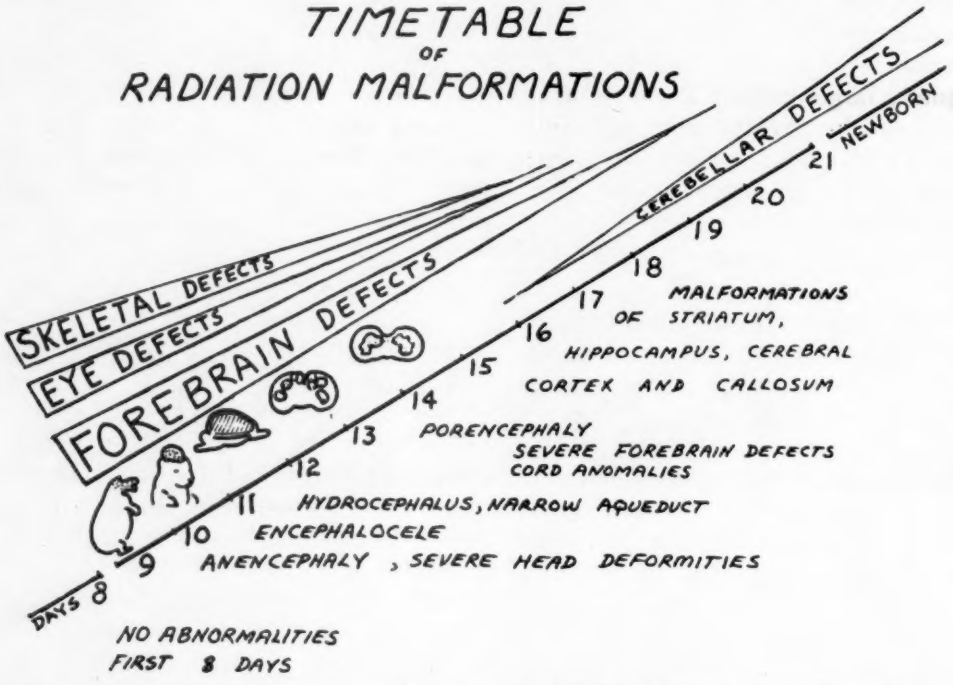

FIG. 14. Timetable of irradiation malformations in rats. The sequence of events described in the experiments is summarized.

trauterine life. Six hundred roentgens simulated the histopathologic effect of the radiomimetic drugs, triethylene melamine and nitrogen mustard, on fetuses, which in substantial dosage attacks not only neuroblasts but cartilage and other cells.[5,6,7] All this suggests that the effect of irradiation on skeletal growth may be two-fold: on the precartilaginous skeletal blastema (destructive?) and the more differentiated embryonal cartilage (altered growth?). Experiments are in progress to examine the nine-ten day period at close intervals to answer some of these questions.

An equally large problem is the detailed correlation of the defects and malformations that are produced in the latter stages of gestation with the parts of the brain that are in the neuroblastic stage. In a general way, the malformations can be recognized as being parallelly related to the successive neuroblastic stages of development of regions of the nervous system as indicated in some descriptions. The details, however, of what cells, for example, form what parts of the corpus callosum, or the cerebellum, on successive days is much less understood. Further, the secondary deficiencies that result from, say, cortical damage in terms of absent fiber tracts in the brain stem and cord have not been worked out. We have worked out very little of the brain stem and spinal cord changes. Still another fruitful line of investigation is a correlation of neurologic and behavior patterns with the malformations present. How some of these animals irradiated in mid-gestation negotiate a fairly "normal" existence, with the brains they have, is a remarkable problem itself.

Another finding of note is the hydrocephalus and narrow aqueduct of the eleventh day. This is being pursued further and might throw considerable light on the problem of human hydrocephalus.

Lastly, diagnosing a mild cerebral malformation in an adult animal is often difficult as opposed to recognizing severe ones. Destruction of a few or even a fair number of neuroblasts in the striatum in its later stages of development can easily go unnoticed without quantitative studies. Loss of a fair number of neuroblasts in the outer cortical zones late in development usually makes its mark as a slight but recognizable deficit and slight jumbling of the nerve cells that do develop. The same amount of damage earlier in cortical development may, however, be very difficult to recognize later, and the deficit is "covered up." The mechanism of this cover-up is by no means solved. It is *partly* due to the fact that the remaining neuroblasts develop a fairly normal structure—the ensuing cortex looks essentially normal, but there is less of it in total extent, for the brain is actually smaller. Whether the neuroblasts can proliferate to compensate their dead brothers and cover up a potential defect by actual replacement is another possibility. In any event, we have seen this phenomenon of cover-up in many litters of animals treated with radiation and such other neuroblasticidal agents such as cortisone, nitrogen mustard, mapharsen, etc. In these, serial examinations of successive members of the litter over a period of time has shown in the acute stage considerable necrosis of neuroblasts, but as time passes the results of the damage become less and less apparent. It is likely that part of the answer will come from quantitative histologic counts, bulk measurements, and detailed studies of cerebral architecture.

CLINICAL IMPLICATIONS

The questions of the relationship of these experiments to human malformations and to pelvic irradiation during human pregnancy have come up frequently. In regard to malformations in general, these and other experiments using certain enzyme inhibitors and hormones suggest that the neuroblast may be the vulnerable point through which a number of agents, presently only suspected, might act in man to produce deformities. The developmental sequences leading to such bizarre growths as anencephaly and encephalocele, and the possible mechanisms of hydrocephalus,

heretofore so difficult to understand, have begun to take shape. Altogether the findings call attention to the importance of effects operating during gestation that may lead to defects.

In respect to the effects of irradiation on the human embryo, it has long been held that pelvic irradiation during early gestation probably causes a variety of defects from microcephaly to eye and skeletal deformities, as indicated by the figures of Murphy[11] and of others. The experimental program described here was initiated in part as a result of our knowledge of a woman with sarcoma of the pelvis who was treated with radiation during early gestation. Here pregnancy resulted in a microcephalic girl now in her teens. The experimental findings that the neuroblast is sensitive in all species tested thus far—rats, mice, hamsters, guinea pigs, ducks, chickens, turkeys—coupled with clinical observations, indicate that the human neuroblast is also radiosensitive. Whether the cell is *equally* sensitive in all mammals is not yet known, so that quantitative application of these animal experiments to human medicine is not possible. In view of the fact that 30 to 40 r damages neuroblasts and alteration of cartilage may occur in a similar or lower range,[5,6,7,13,14] this order of magnitude might serve as a point of departure for estimating clinical risks. Such a reference figure might be a useful guide when series of roentgenologic studies involving the abdomen and pelvis is contemplated in young women who might be in the early stages of pregnancy.

A correspondence of embryo ages between species with different gestational periods can only be approximated. First somites appear in the human at about sixteen days, in the rat about the ninth day. In the rat or mouse the next few days see rapid and substantial development of organ systems toward the adult pattern whereas in the human a comparable stage is not attained until the embryo is perhaps five or six weeks old. Thereafter, the human differential developmental pattern becomes relatively slower and slower and the differences between man and the animal become more and more apparent. The rat at birth corresponds roughly to a late human fetus. At three weeks of age (postnatal) the rat brain is virtually mature in terms of differential growth, and the animal may reproduce before it is three months old. Thus, close comparisons of development can be approximated only in the early stages.

It is noteworthy, however, that the radiosensitivity of a given type of cell—the neuroblast, for example—continues at substantially the same low level throughout the period of fetal and newborn development of the animal. If there is a risk early in human gestation from an arbitrarily selected level of irradiation, then the risk of damage must also be present throughout the embryonal developmental period. Only the *pattern* of damage would change. It is perhaps significant to note in this connection that malformations in the rat acquired late in gestation or after birth are easily overlooked on casual external observation, but a closer scrutiny by neurologic and pathologic examination reveals them to be serious.

SUMMARY

The malformations, especially those of the nervous system, produced in developing rats by giving single doses of radiation to the pregnant mothers on successive days during gestation are presented. The embryologic mechanisms are discussed and illustrated and a timetable is presented.

No deformities occurred following irradiation in the first eight days of gestation. Anencephaly and multiple head defects occurred on the ninth day, encephalocele and craniocerebral defects on the tenth, eleventh, and twelfth days, with hydrocephalus and narrow aqueduct being characteristic of the eleventh day. The thirteenth through sixteenth days showed severe cerebral and striatal malformations. Little or no corpus callosum developed following irradiation on any day from the

ninth to nineteenth days. Striatal, hippocampal and cortical defects were decreasingly severe as injury was induced on successive days in the latter third of gestation. The cerebellum began to show increasing damage as the radiation was given on days approaching term and in the postnatal period. Skeletal and eye deformities occurred in the ninth to fourteenth day period especially.

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A NOTE ON THE BRAIN CLIP AS AN AID IN ESOPHAGEAL DIAGNOSIS

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WASHINGTON, D. C.

THE endoscopist is able with considerable precision to localize a lesion within the esophagus, by measuring against the instrument its distance from the superior alveolar ridge. As important as such a measurement is for the endoscopist's own purposes, however, it is not particularly helpful when the esophagoscopic findings are being compared with those of the radiologist. It is especially when the latter are interpreted as normal that the translation of linear measurements to the roentgenologic picture may fail to enable the radiologist to understand the exact site of suspected disease.

The trans-esophagoscopic attachment of a brain clip to the esophageal mucosa at the site of a lesion or at the site of a trans-esophagoscopic biopsy has proved of considerable help in certain diagnostic problems. Roentgenologic study of the chest made after the clip is in place permits permanent recording of the point of reference for subsequent contrast and other study.

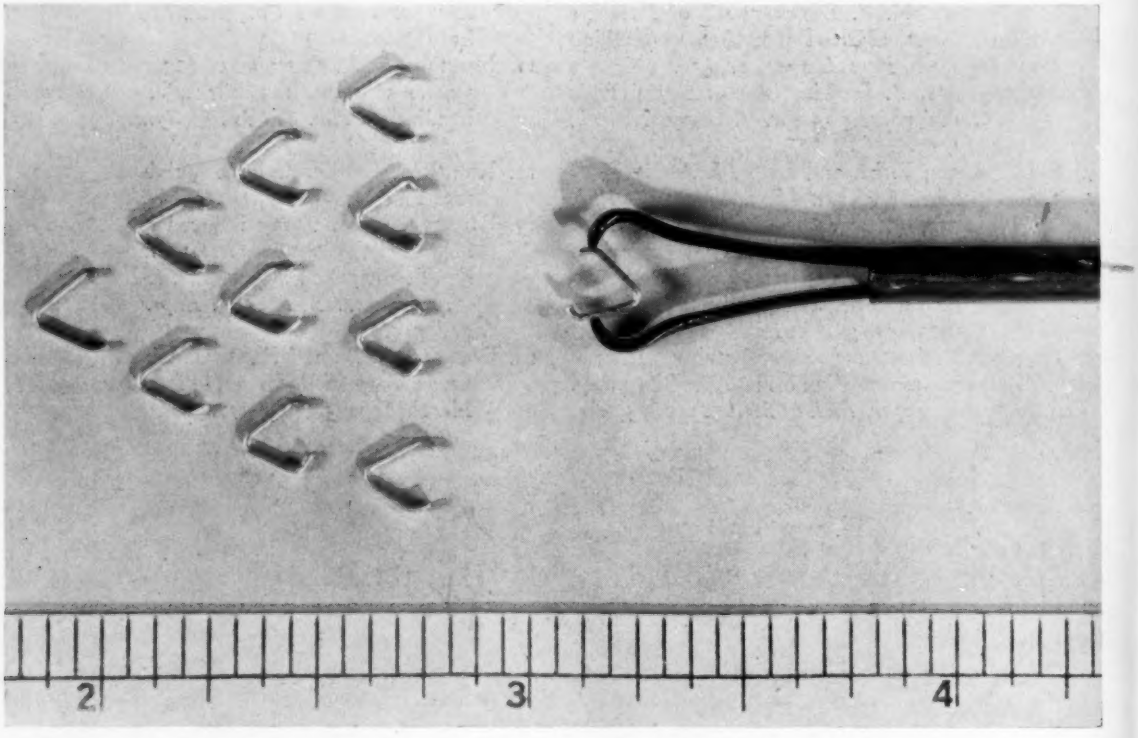

FIG. 1. Brain clips prepared for esophageal use. The right angle turning forceps is loaded, ready for use. (The scale is in inches.)

TECHNIQUE

Silver brain clips are prepared so that they will grasp the esophageal mucosa, by bending the tips toward each other in the fashion of a skin clip (Fig. 1). If the clip is to be carried in

forceps with corregated jaws, such as the fenestrated peanut forceps, no further preparation is necessary. The right angle turning forceps is satisfactory, but, in order that the clip be carried securely in this instrument, it is necessary to crease the surface of each of the square ends cannot pierce the epithelium. The malleability of the soft silver wire used in the clip leads to collapse of its shafts as resistance is met between the jaws.

The patient must be sent to the radiologist within an hour or two, for the clip soon becomes

Fig. 2. Esophagoscopic view of clip in place. A small amount of mucosa has been caught up, and the clip's prongs have buckled under the resistance met in the mucosa.

clip's prongs by a gentle squeeze between the jaws of ordinary shop pliers.

The actual technique of placing the clip is not at all difficult, although a second attempt may at times be necessary because of failure to grasp the mucosa. At the completion of the examination, the clip is merely carried through the esophagoscope to the selected site and squeezed onto the surface. A small amount of mucosa is picked up automatically between the jaws of the clip (Fig. 2). No bleeding has been encountered, and it is thought that the clip's detached and is lost into the intestine. A small meal will usually release it, and rarely will it be found in place the day following esophagoscopy. A left anterior oblique film is most satisfactory for recording the marked area (Fig. 3).

COMMENT

This technique has been particularly useful for marking the upper limit of esophageal varices as observed esophagoscopically, and in designating the exact

Fig. 3. The roentgenologist obtains a permanent record of the precise location of the point indicated by the esophagoscopist.

level of ampullary ulcers. At times it has proved helpful to mark the esophagogastric junction in instances of sliding hiatus hernia, and to make a record of the exact site from which a biopsy was taken. Discussion between radiologist and esophagoscopist over certain diagnostic problems has been facilitated considerably thereby, with a degree of increased diagnostic accuracy.

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Thirty-fifth Annual Meeting: Chase Hotel, St. Louis, Mo., April 20, 21 and 22, 1953.

EDITORIAL

THE ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE Thirty-fifth Annual Meeting of the American Radium Society will be held on April 20, 21, 22, 1953, in St. Louis, Missouri, at the Park Plaza Hotel and Chase Hotel. Every radiologist concerned with radiotherapeutics in any of its various forms will find the program interesting and instructive. All are cordially invited to attend this meeting. The program covers therapeutic modalities from roentgen rays to neutrons and regional neoplasms from the brain to the uterine cervix, indicating the broad scope and varied interests of the American Radium Society.

The scientific program covers a period of two and one-half days. About twenty formal papers will be presented during two days while the remaining half day will be devoted to clinics at the nearby Washington University School of Medicine. Washington University is celebrating its Centennial Anniversary this year. Of the formal program about one-half day will be devoted to each of the following general topics—practical aspects of radiation physics, carcinoma of the uterus, lesions of the head and neck, and miscellaneous problems in radiotherapeutics. The presentations at Washington University will comprise technical demonstrations and clinical case presentations. Technical demonstrations will include introduction of radiogold into the prostate and into the parametria, demonstration of various fixed radium applicators and the direct measurement of pelvic irradiation. The tumor clinic will provide actual cases to be evaluated and discussed by a panel of experts representing radiology, surgery and pathology.

The Janeway Lecture will be presented in conjunction with a luncheon in the beautiful Tiara Room at the top of the Park Plaza. The cocktail hour and banquet will be held on the Starlite Roof and in the Zodiac Room of the Chase. A barbecue picnic lunch sponsored by the St. Louis Radiological Society will be held Wednesday noon in the Lazy M. D. Corral at the residence of Dr. Edwin C. Ernst.

All those interested should plan to attend the meeting of the American Radium Society in St. Louis during April. The location is central, the weather is usually balmy and the three day meeting will provide inspiration and relaxation. The interconnecting Chase Hotel and Park Plaza Hotel, beautifully located on the park, provide superb facilities for the meeting. Reservations may be arranged through Mr. E. J. Hoelscher, Chase Hotel, 212 N. Kingshighway, St. Louis, Missouri.

HOWARD B. HUNT, M.D.
President

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 29–Oct. 2, 1953.

American Radium Society
Secretary, Dr. J. E. Wirth, 635 Herkimer St., Pasadena 1, Calif. Annual meeting: Chase Hotel, St. Louis, Mo., April 20–22, 1953.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: 1953, to be announced.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: 1953, to be announced.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 15 E. Monroe, Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. William Curtis, 1612 Tremont, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. J. C. Cook, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. A. Judson Graves, 2002 Park St., Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert M. Tankesley, 218 Doctors Bldg., Atlanta, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Miami Radiological Society
Secretary, Dr. Maurice Greenfield, Ingraham Bldg., Miami, Fla. Meets third Wednesday of each month at Veterans Administration Building.

Houston Radiological Society
Secretary, Dr. F. M. Windrow, 1205 Hermann Professional Bldg., Houston, Texas. Meets fourth Monday each month.

Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. James McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. Willis L. Beeler, M.D., 700 Kansas Ave., Topeka, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Marcus Wiener, 1430 48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Joseph F. Linsman, 436 N. Roxbury Dr., Beverly Hills, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. Hugh Allan Smith, Eastern Maine General Hospital, Bangor, Maine. Meets in early spring, June and fall.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. John W. Evans, 621 High Street, Jackson 2, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Will meet at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph J. La Vine, 259 North Grand Ave., Baldwin, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. R. W. Blanchard, 1216 Medical Arts Bldg., Omaha, Nebr. Meets fourth Thursday of each month at 6 P.M. at Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Harold W. Jacox, 622 W. 168th St., New York 32, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. John F. Roach, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April. Annual meeting will be held in May or June, 1953.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. Richard C. Ripple, 1215 28th Street, Sacramento, Calif. Meets at dinner last Monday of September, November, January, March and May.

OHIO STATE RADIOLOGICAL SOCIETY
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Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. J. Richard Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. George P. Keefer, American Oncologic Hospital, Philadelphia 4, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets 6:00 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

RADIOLOGICAL SECTION, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary, Dr. U. V. Wilcox, 915 Nineteenth St., N. W., Washington 6, D. C. Meets Medical Society Library, third Thursday of January, March, May and October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Harry K. Hines, 2508 Auburn Ave., Cincinnati 19, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Colonel Alexander O. Haff, M.C., Tripler Army Hospital, Honolulu, T. H. Meets third Friday of each month at Tripler Army Hospital.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Nicholas G. Demy, 912 Park Avenue, Plainfield, N. J. Meets annually at Atlantic City at time of State Medical Society and mid-winter at Elizabeth, N. J.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Robert J. Bloor, 260 Crittenden Blvd., Rochester, N. Y. Meets last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Next annual meeting, Shirley-Savoy Hotel, Denver, Colo., August 20, 21 and 22, 1953.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. Francis O. Trotter, Jr., 634 N. Grand Blvd., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August and September.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

SAN DIEGO RADIOLOGICAL SOCIETY
Secretary, Dr. Rex Uncapher, 7720 Girard Ave., La Jolla, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

SECTION ON RADIOLOGY. CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. Calvin L. Stewart, 2330 First Ave., San Diego 1, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Bay Radiological Society
Secretary, Dr. Ford Shepherd, 526 Soquel Avenue, Santa Cruz, Calif. Meets second Wednesday each month.

South Carolina Radiological Society
Secretary, Dr. Henry E. Plenge, Spartanburg General Hospital, Spartanburg, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, Newell Hospital, Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. John N. Burkey, 555 Medical-Dental Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May.

Westchester Radiological Society
Secretary, Dr. Walter J. Brown, Northern Westchester Hospital, Mt. Kisco, N. Y. Meets on third Tuesdays of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. Irving I. Cowan, 425 E. Wisconsin Ave., Milwaukee 2, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. Charles E. Duisenberg, Palo Alto Clinic, 300 Homer Ave., Palo Alto, Calif. Meets third Thursday at 7:45 P.M., January to June, Lane Hall, Stanford University Hospital; July to December, San Francisco Hospital.

Cuba, Mexico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiologia y Fisioterapia
General Secretary, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. Jean Bouchard, Suite 305, 1555 Summerhill Avenue, Montreal 26, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electrologie et de Radiologie Médicales
Secretary, Dr. Origéne Dufresne, 4120 Ontario St., East Montreal, P. Q.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro Sede, Cordoba
President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Alberto Torres Focke, Av. 34, No. 17-34, Bogota, Colombia. Meets last Wednesday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

CONTINENTAL EUROPE

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

SOCIÉTÉ FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALE, and its branches: SOCIÉTÉ DU SUD-OUEST, DU LITTORAL MÉDITERRANÉEN, DU CENTRE ET DU LYONNAIS, DE L'OUEST, DE L'EST, ET D'ALGER ET D'AFRIQUE DU NORD
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX°, France.

CESKOSLOVENSK SPOLEČNOST PRO RËNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

WROCŁAW SECTION POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

DEUTSCHE ROENTGEN-GESELLSCHAFT
Secretary, Dr. Peter Kröker, (22a) Essen-Helsingen, Westpreussenstrasse 21. Meets annually in different towns.

SOCIETA ITALIANA DR RADIOLOGIA MEDICA
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

INDIA

INDIAN RADIOLOGICAL ASSOCIATION
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

PRELIMINARY PROGRAM

AMERICAN RADIUM SOCIETY

THE following is the tentative program which has been arranged for the Thirty-fifth Annual Meeting of the American Radium Society which will be held at the Park Plaza and Chase Hotels, St. Louis, Missouri, on Monday, Tuesday and Wednesday, April 20, 21, and 22, 1953.

Monday, April 20, 1953
Zodiac Room, Chase Hotel

8:30 A.M. Registration, Entrance to Zodiac Room.
9:00 A.M. Executive Session.
9:05 A.M. Address of Welcome.
Scientific Session. Chairman: Wendell G. Scott, M.D., St. Louis, Mo.
9:10 A.M. Presidential Address. Howard B. Hunt, M.D., Omaha, Nebr.
9:30 A.M. Radiation Therapy in Carcinoma of the Floor of the Mouth. Harry Hauser, M.D., Cleveland, Ohio.
9:50 A.M. Discussion.
9:55 A.M. The Management of Tumors of the Parotid Gland. Irving Abriel, M.D., Anthony Jerome, M.D., and George T. Pack, M.D., New York, N.Y.
10:15 A.M. Discussion.
10:20 A.M. Melanoma of the Head and Neck. Daniel Catlin, M.D., New York, N. Y.
10:40 A.M. Discussion.
10:45 A.M. Chemosurgery in Cancer Persistent or Recurrent Following Irradiation. Frederick E. Mohs, M.D., Madison, Wis.
11:05 A.M. Discussion.
11:10 A.M. Radiostrontium in Diseases of the Eye. Hymer L. Friedell, M.D., Cleveland, Ohio.
11:30 A.M. Discussion.
12:00 A.M. Janeway Luncheon and Lecture, Tiara Room, Park Plaza Hotel. Chairman: Douglas Quick, M.D., New York, N. Y.
2:00 P.M. Executive Session. Zodiac Room.
Scientific Session. Chairman: Edith H. Quimby, D.Sc., New York, N. Y.
2:20 P.M. Treatment Planning in Roentgen Therapy. Robert J. Bloor, M.D., and Raymond S. Quick, B.Sc., Rochester, N. Y.
2:40 P.M. Discussion.
2:45 P.M. Physical Factors in the Use of Cobalt 60 in Interstitial and Intracavitary Therapy. Gilbert H. Fletcher, M.D., Peter Wootton, B.Sc., and Robert J. Shalek, M.A., Houston, Tex.
3:05 P.M. Discussion.
3:10 P.M. Dosimetric Calculations from Roentgenograms in Radium Therapy of Carcinoma of Cervix Uteri. Franklin L. Payne, M.D., Philadelphia, Pa.
3:30 P.M. Discussion.
3:35 P.M. The Value of Serial Isotope Tracer Studies in the Differential Diagnosis of Upper Mediastinal Tumors. Kenneth E. Corrigan, Ph.D., H. S. Hayden, Ph.D., and James C. Cook, M.D., Detroit, Mich.
3:55 P.M. Discussion.
4:00 P.M. Functions of the Hospital Physicist. Herbert M. Parker, Ph.D., Richland, Wash.
4:20 P.M. Discussion.
7:00 P.M. Cocktails, Starlite Roof, Chase Hotel.
8:00 P.M. Banquet, Zodiac Room.
10:00 P.M. Dancing, Chase Club.

Tuesday, April 21, 1953
Regency Room, Chase Hotel

9:00 A.M. Executive Session.
Scientific Session. Chairman: J. Ernest Breed, M.D., Chicago, Ill.
9:10 A.M. Roentgen Therapy of Hepatic Metastases. Ralph F. Phillips, M.D., New York, N. Y.
9:30 A.M. Radiation Treatment of Pulmonary Metastases. Wendell G. Scott, M.D., William Moss, M.D., and David R. Rich, M.D., St. Louis, Mo.
9:50 A.M. Discussion. Lemuel Bowden, M.D., New York, N. Y., and Angus K. Wilson, Salt Lake City, Utah.

10:00 A.M. Roentgen Therapy of Medulloblastoma. Carleton B. Peirce, M.D., and Jean Louis Bouchard, Montreal, Canada.

10:20 A.M. Neutron Bombardment of Boron in Treatment of Brain Tumors. Lee E. Farr, M.D., Brookhaven, N. Y.

10:40 A.M. Discussion.

10:50 A.M. Radiogold in Intracavitary Carcinomatosis. Morton M. Kligerman, M.D., New York, N. Y.

11:10 A.M. Discussion. Henry L. Jaffe, M.D., Los Angeles, Calif.

11:20 A.M. The Future of Therapeutic Radiology. Justin J. Stein, M.D., Los Angeles, Calif.

11:40 A.M. Comparison of Radiotherapy Abroad and in the United States. Robert E. Fricke, M.D., Rochester, Minn.

12:00 A.M. Discussion.

2:00 P.M. Executive Session.
Scientific Session. Chairman: Howard B. Hunt, M.D., Omaha, Nebr.

2:20 P.M. Radium Dosimetry in Carcinoma of Corpus Uteri. R. K. Leffler, M.D., and Vincent P. Collins, M.D., Houston, Tex.

2:40 P.M. Discussion.

2:45 P.M. Management of Carcinoma of Cervical Stump. Ralph M. Caulk, M.D., Washington, D. C.

3:05 P.M. Discussion.

3:10 P.M. Correlation of Radiotherapeutic Dosage with Results in Carcinoma of Cervix Uteri. Manuel Garcia, M.D., New Orleans, La.

3:40 P.M. Interstitial Radium Treatment of Carcinoma of the Cervix; Clinical Appraisal. James A. Corscaden, M.D., New York, N. Y.

4:00 P.M. Discussion.

4:05 P.M. Augmentation of Radiotherapeutic Response in Carcinoma of Cervix Uteri by Intravenous Aureomycin. Jeanne C. Bateman, M.D., Charlotte P. Donlan, M.D., Keith Cramer, M.D., and Calvin T. Klopp, M.D., Washington, D. C.

4:25 P.M. Discussion.

Wednesday, April 22, 1953
Wohl Auditorium, Washington University, School of Medicine

Scientific Session. Chairman, A. N. Arneson, M.D., St. Louis, Mo.

9:00 A.M. Parametrial Implantation of Radioactive Gold in Carcinoma of Cervix Uteri. Willard M. Allen, M.D., and Alfred I. Sherman, M.D., St. Louis, Mo.

9:20 A.M. Intracapsular Injection of Radiogold in Cancer of Prostate. H. B. Elkins, M.D., *et al.*, Iowa City, Iowa.

9:40 A.M. Fixed Radium Applicators for Carcinoma of Cervix. Edwin C. Ernst, M.D., Alfred I. Sherman, M.D., and Michel Ter-Pogossian, Ph.D., St. Louis, Mo.

10:00 A.M. Measurement of Radiation in the Pelvis with Scintillation Counter. John A. Wall, M.D., and Gilbert H. Fletcher, M.D., Houston, Tex.

10:30 A.M. Cancer Clinic arranged by William Moss, M.D., St. Louis, Mo. Discussion will be presented by a panel of experts representing radiology, pathology and surgery.

12:00 A.M. Executive Session.

1:00 P.M. Barbecue Luncheon at Lazy M.D. Corral, Residence of Dr. Edwin C. Ernst. Sponsored by St. Louis Radiological Society.

RADIOLOGICAL AWARD GIVEN TO DR. ROSS GOLDEN

The Gold Medal of the Radiological Society of North America was presented to Dr. Ross Golden of New York City at the annual banquet of the Society held on December 11, 1952, during the annual meeting in Cincinnati. The Medal, awarded "for outstanding achievement in the field of radiology," was presented by Dr. Joseph C. Bell, retiring President of the Society. Dr. Golden, who is Professor of Radiology at Columbia University and Editor of *Diagnostic Radiology*, is also widely known for his research on the human small intestine and for his numerous other contributions to the advancement of radiology.

POSTGRADUATE COURSE IN RADIOLOGY

A postgraduate course in radiology has been

arranged at the University of Kansas Medical Center with the active cooperation of the Radiological Society of Greater Kansas City and the Kansas Radiological Society and with the generous participation of the members of both organizations. This is to be held on February 16, 17 and 18, 1953. The course will endeavor to present at least a brief summary of the field of radiology in the diagnosis and treatment of all branches of medicine and surgery. The program on Monday and Tuesday covers a wide variety of fields in diagnosis, and the program on Wednesday is devoted almost exclusively to therapy. This is arranged as the official meeting of both the Radiological Society of Greater Kansas City and the Kansas Radiological Society.

Further information concerning the course may be obtained from the Extension Program in Medicine, University of Kansas Medical Center, Kansas City, Kansas.

POSTGRADUATE COURSE IN DISEASES OF BONES AND JOINTS

A postgraduate course in roentgenographic interpretation of the diseases of bones and joints will be given by Dr. Maurice M. Pomeranz, Director of Radiology at the Hospital for Joint Diseases, Madison Avenue at 123rd Street, New York City, in affiliation with Columbia University College of Physicians and Surgeons from March 4, 1953, through May 20, 1953.

There will be a series of lectures covering the roentgenographic analysis of acute and chronic diseases of bones and joints including granulomas, neurotrophic lesions, neoplasms, and the manifestations of nutritional and metabolic bone changes in children and adults.

The course will consist of a didactic lecture lasting about one hour and followed by a lantern slide demonstration illustrating the disease or diseases under discussion. An average of approximately thirty-five to fifty lantern slides will be shown at each session, all representing material selected from cases seen at the Hospital for Joint Diseases during the past twenty-five years.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

At the Thirty-eighth Annual Meeting of the Radiological Society of North America held in Cincinnati on December 7–12, 1952, the following officers were elected for 1952–1953: *President-Elect*, Dr. Eugene P. Pendergrass, Philadelphia, Pennsylvania; *First Vice-President*, Dr. Charles H. Heacock, Memphis, Tennessee; *Second Vice-President*, Colonel Harold I. Amory, Medical Corps, A.U.S., Washington, D.C.; *Third Vice-President*, Dr. Leslie K. Sycamore, Hanover, New Hampshire; *Secretary-Treasurer*, Dr. Donald S. Childs, Syracuse, New York (re-elected). Dr. Ira H. Lockwood, Kansas City, Missouri, took office as *President* of the Society.

RESIDENCIES IN EXPERIMENTAL MEDICINE

The Medical Division of the Oak Ridge Institute of Nuclear Studies is inviting applications for one-year residencies in experimental medicine. Two appointments will be made annually beginning in 1953.

The Division operates under contract with the U. S. Atomic Energy Commission a 30-bed research hospital and extensive laboratories for correlation of basic scientific studies with clinical investigation. An active research program of experimental cancer therapy with radioisotopes is in progress under the direction of a full-time staff and consultants from participating medical schools. Research in progress offers opportunities for metabolic studies with isotopes and for investigations in the field of hematology.

The residencies are approved for one year of basic credit in Internal Medicine by the American Medical Association and the American Board of Internal Medicine. Stipends are $2,000 plus $4 a day subsistence in lieu of maintenance.

Additional information may be obtained from Marshall Brucer, M.D., Chairman, the Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee.

POSTGRADUATE COURSE ON MOVING FIELD THERAPY

The Medical University Clinic, Erlangen (West Germany), is planning a postgraduate course on moving field therapy (rotation, pendulum, and convergent beam therapy) for those who are interested and do not speak the German language. The course will be held from August 3 to 8, 1953, following the Seventh International Congress of Radiology in Copenhagen, Denmark, July 19–25, 1953. Reports will be given in English and Spanish only. In addition, planning of treatment techniques and treatment of patients will be demonstrated in practice. The fee is DM 75.-. Further details may be obtained by writing to Sekretariat des Fortbildungskurses für Bewegungsbestrahlung, Medizinische Universitätsklinik, Krankenhausst. 6, Erlangen, West Germany.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

AN ATLAS OF GENERAL AFFECTIONS OF THE SKELETON. By Sir Thomas Fairbank, D.S.O., O.B.E., M.S., Hon. M.Ch. (Orth.), F.R.C.S., Consulting Orthopaedic Surgeon and Emeritus Lecturer in Orthopaedic Surgery, King's College Hospital; Consulting Surgeon, Hospital for Sick Children, Great Ormond Street; Emeritus Consulting Surgeon, Lord Mayor Treloar Orthopaedic Hospital, Alton; Honorary Consultant (Orthopaedic) to the Army. Cloth. Price, $10.00. Pp. 411, with 184 illustrations. Williams & Wilkins Company, Mt. Royal and Guilford Avenues, Baltimore 2, Maryland, 1951.

The author of this Atlas has taken an interest for many years in affections of the skeleton that show multiple lesions. He has now made available to others some of the information, gleaned from his collection of records and cases, with the hope that it may be of assistance in the diagnosis of various affections, many of which are uncommon.

In the Introduction, he gives a classification of the general affections of the skeleton according to their etiology which is followed with but few exceptions. These exceptions were made because he considered it advantageous to consider some of them with affections of an entirely different etiology because of certain similarities which they show. Tables are included giving the classification of the general affections of the skeleton; a list of diseases showing dwarfism, of the short limb type and of the short trunk type; a list of diseases causing increased density of more than one bone; a list of those causing collapse of one or more vertebrae, and those causing multiple fractures, more or less spontaneous. The affections of the skeleton which show changes in the eyes are listed, also asymmetry of the face, cutaneous abnormalities, symmetrical enlargement of the lower thirds or more of the femora, indentations of the pelvis, separation of the epiphyses, irregular ossification of the epiphyses and fibrosis of the bone marrow.

The book is of convenient size for reading and the text is well arranged. Some of the chapters were first published in the *Journal of Bone and Joint Surgery*. The references are not too numerous but are well chosen. The author calls attention whenever possible to one or two articles which he thinks comprise good résumés of the disease under discussion. He has also included in the limited number of references reports of unusual features or complications of exceptional interest or importance. No discussion of treatment of the diseases is given.

The text is illustrated with numerous roentgenograms. They are, with few exceptions, printed positives. As a result, in some instances there is a loss of bone detail, especially in the sclerotic areas of involvement. A few line drawings of bone changes in rare conditions and a few illustrations of microscopic sections complete the illustrations.

Among the rare diseases described are osteopathia striata, generalized hyperostosis with pachyderma, Léri's pleonostosis, ateliosis (sexual), familial metaphyseal dysplasia and dysplasia epiphysialis multiplex.

The roentgenologist will find this a most useful reference book and also a book well worth serious study, not only because of the descriptions of the various diseases but also because of the illustrative roentgenograms. In addition, he may find described the rare condition which he is seeking and a time-consuming search of the literature may be avoided. It cannot be too highly recommended.

RALPH S. BROMER, M.D.

THE PATHOLOGY OF PATIENTS. INCLUDING DISCUSSIONS OF BASIC PHOTOGRAPHIC AND OPTICAL PRINCIPLES. By H. Lou Gibson, F.B.P.A., A.P.S.A., Medical Division, Eastman Kodak Company, Rochester, New York. Cloth. Price, $5.50. Pp. 118, with numerous illustrations. Charles C Thomas, Publisher, 301 East Lawrence Avenue, Springfield, Illinois, 1952.

The text of this splendid little book is obviously directed toward the physician who does occasional clinical photography rather than toward the professional photographer. For this reason, it deserves more than casual attention

from interested members of the medical profession.

The book contains more than the usual amount of technical information presented in an orderly and thoroughly understandable manner, with unnecessary and highly involved aspects either simplified or omitted. For example, lens theory is handled in a basic but adequate fashion, and the aura of mysticism commonly associated with a discussion of such terms as "gamma," "gradient" and "resolving power" has been largely removed.

Easy readability, superb illustrations and concise, practical exposure tables are additional features for which the author and publisher are to be commended. One might criticize the omission of any mention of background colors in color photography, the practice of retouching negatives and the use of the increasingly popular speed light, but subject material of this sort is, after all, more in the realm of professional photography.

Lest radiologists be misled, it should be emphasized that no specific data concerning the photographing of roentgenograms is included but, of course, many of the basic principles apply.

John F. Holt, M.D.

Einführung in die Röntgenologie. Ein Lehrbuch für Ärtze und Studierende. Von G. F. Haenisch, A. O. Prof. Dr. Med., Chefarzt I.R. am allgem. Krankenhaus, Barmbeck, Hamburg; und H. Holthusen, O. Ö. Prof. Dr. Med., Chefarzt am allgemeinen Krankenhaus, St. Georg, Hamburg. Mit einem physikalisch-technischen Beitrag von A. Liechti, bearbeitet und ergänzt von Dr. W. Fehr, Hamburg. Fünfte, erweiterte Auflage. Cloth. Price, DM 60.-. Pp. 521, with numerous illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany, 1951.

In their introduction the authors of this text state that their purpose is to familiarize the reader with the fundamental aspects of radiology. The work is divided into three parts of which the first, by Prof. A. Liechti—revised after his death by W. Fehr, Hamburg—is a brief review of roentgen-ray physics and apparatus, and of film processing; the second, on diagnosis, by Prof. G. F. Haenisch, and the third dealing with therapy, by Prof. H. Holthusen, comprise the major part of the book.

In the first section Liechti, after briefly reviewing the physics of electricity, including alternating current, induction and transformers, outlines roentgen-ray physics at somewhat greater length without, however, going into detail or touching on its refinements. Included in this section is a dicsussion of the interaction of roentgen rays and matter. The writer states well known principles of absorption and scattering, giving brief explanations of these phenomena. He describes the various types of roentgen tubes and their structure, methods of rectification, voltage regulating and other apparatus. He also mentions special equipment such as stereoscopes, Potter-Bucky diaphragms, laminagraphs, kymographs, and high voltage equipment. He devotes a small section to protection, and since this part is quite general in scope, he refers the reader to two German handbooks on this subject.

The section on diagnosis comprises almost half the book; in general, the writer, Haenisch, follows established textbook methods of presenting his material. After an introductory explanation of roentgenographic principles and a discussion of indications for roentgenoscopy and roentgenography he describes the normal roentgenographic appearances of the skeleton, thorax, heart and the gastrointestinal tract. He gives as examples of the normal skeletal system views of some portions of the skeleton but makes no attempt to include all parts or even most of the skeletal structure, and therein this work differs from the usual text on general roentgen diagnosis. The illustrations are uniformly excellent, although they are positive, not negative, reproductions. Many are accompanied by line tracings and the latter are notable for their clarity, but would be of greater value to the average non-radiologic physician if their parts were labeled.

Haenisch includes a discussion of methods of enhancing differences in density in the examination of hollow viscera and gives a brief comprehensive historical review of the use of air and other contrast material.

The remainder of the diagnostic section of this book concerns itself generally with diseases of the various body systems. Each is taken up categorically, and the more common entities are described, *i.e.*, the osseous system including inflammatory processes, avitaminoses, aseptic necroses, disturbances in calcification, arthritides, tumors, benign and malignant, heterotopic ossification and calcification, congenital deformities, and fractures. In a similar

manner common pathologic affections of the gastrointestinal, urogential, cardiovascular, and pulmonary systems are described.

In general, Haenisch presents the subject matter concisely and clearly, if somewhat encyclopedically. Differing viewpoints are not given and little attempt is made to correlate roentgen appearances with histopathologic findings. But, on the whole, these are minor criticisms, since—to paraphrase the writer—the object of the text is to acquaint the reader with fundamental concepts, so that he will recognize the value and applicability as well as the limits of diagnostic roentgenology.

The section on radiation therapy has been completely rewritten by Holthusen. In view of the tremendous advances made in this field of medicine the discussion is not limited to roentgen therapy alone but the subject matter is presented from the viewpoint of the characteristics and actions of ionizing radiations in general.

Following a brief historical introduction the author relates the properties of ionizing radiations (roentgen rays, electrons, alpha rays, neutrons, also radium and radioisotopes) and their measurement. The biologic effects of these rays are discussed in detail, since a thorough understanding of this subject is the very basis of radiation therapy. This section includes a description of the systemic effects of irradiation, radiation injuries and their prevention. Very interesting is the portion that deals with the time factor; the importance of its bearings on clinical radiation therapy cannot be overemphasized.

This general part of the therapeutic section is followed by a special part outlining the treatment methods customarily used today. Holthusen presents rules regarding the choice of the quality of radiation, the dose, and the execution of the treatment plan. This is followed by a discussion of radiation therapy of various diseases and organ systems: skin, inflammatory disease, bone and joints, blood forming organs and lymph nodes, benign lesions of the female genital organs, glands of external and internal secretion, nervous system; malignant and benign tumors, and hyperplasias. A highly informative section is found in the discussion of malignant disease which may well be labeled: What can we expect from radiation therapy of various neoplasams? In it the author presents in table form the average percentage of five year arrests to be expected from radiation therapy in malignant neoplasms. The figures are for skin (untreated basal cell carcinoma) 80–90 per cent; larynx (early cases) 80 per cent; skin (absolute cures) 61–70 per cent; lip 60–70 per cent; seminoma (25 of 44 cases) 60 per cent; carcinoma of the fundus (based on Heyman's 475 cases) 60 per cent; penis (31 own cases) 55 per cent; female urethra (27 own cases) 50 per cent; breast (relative cures) 42 per cent; cervix (8,366 cases) 39–40 per cent; larynx (absolute cures) 33–36 per cent; vagina (357 cases) 27 per cent; nasopharynx 25–30 per cent; breast (absolute cures) 25 per cent; tonsil 25 per cent; tongue 17–22 per cent; oropharynx 15–21 per cent; hypopharynx 10–17 per cent; breast (recurrence) 15 per cent.

The illustrations are well chosen and of high quality. Although the book is meant as an introduction to roentgenology for the beginner, the reviewers feel that even the experienced will profit by its perusal.

E. A. Pohle, M.D.
T. A. Gross, M.D.

Peptic Ulcer. Clinical Aspects, Diagnosis, Management. David J. Sandweiss, M.D., F.A.C.P., Editor, Associate Attending Physician, Division of Internal Medicine, Harper Hospital, Detroit, Michigan. Editorial Committee: A. H. Aaron, Henry L. Bockus, George E. Daniels, George B. Eusterman, L. Kraeer Ferguson, A. C. Ivy, Sara M. Jordan, Frank H. Lahey, Walter L. Palmer, Harry Shay, Albert M. Snell, and Dwight L. Wilbur. Cloth. Price, $15.00. Pp. 790, with 164 illustrations. W. B. Saunders Company, West Washington Square, Philadelphia 5, Pennsylvania, 1951.

In sponsoring this publication The American Gastroenterological Association has done medicine a distinct service. For now, gathered together in one volume, is almost everything one should know about the clinical aspects, diagnosis and management of peptic ulcers as it stands in 1951.

David J. Sandweiss is its Editor. He has done a magnificent job of welding together an apparently endless amount of material. He has given the book a continuity in thought which makes easy and interesting reading of a wealth of information that might easily have proved dull and overwhelming. As Sandweiss has indicated, credit for the finished product is due his Editorial Committee which includes such well known names as Aaron, Bockus, Daniels,

Eusterman, Ferguson, Ivy, Jordan, Lahey, Palmer, Shay, Snell and Wilbur.

"Peptic Ulcer" is divided into eight sections:

I. Anatomy and Physiology of the Upper Gastro-Intestinal Tract
II. Pathogenesis and Etiology of Peptic Ulcer
III. Diagnosis and Differential Diagnosis of Uncomplicated Gastroduodenal Ulcer
IV. Medical Treatment of Uncomplicated Gastroduodenal Ulcer
V. Surgical Treatment of Gastroduodenal Ulcer
VI. Peptic Ulcer of the Young and the Aged
VII. Peptic Ulcer Other Than Gastroduodenal Ulcer
VIII. Complications of Gastroduodenal Ulcer

Each "section" is made up of a group of "chapters" submitted by well recognized authorities, 77 in all. In most instances the authors have previously been identified in the literature with the material they are presenting, giving thereby added significance to their contributions.

It appears that nothing was omitted. There are areas to which greater emphasis might have been given, and others which seem overemphasized. This is a personal reaction which will vary with the interests of the reader.

The index merits special comment. It is unusually complete. The author index is also excellent.

The book is printed upon good paper and the type permits easy reading. It contains 790 pages of which the 64 chapters occupy 695 pages, the index 86 pages, and the author index, 9 pages. Each chapter includes its own bibliography which in some instances number as many as fifty to sixty references. It is a volume which should have wide acceptance. We recommend it highly.

PHILIP J. HODES, M.D.

TUMORS OF THE SKIN, BENIGN AND MALIGNANT. By Joseph Jordan Eller, B.S., M.D., Director of the Department of Dermatology, New York City Hostipal, New York, etc.; and William Douglas Eller, M.D., Assistant in Dermatology and Syphilology, University Hospital, New York-Bellevue Medical Center, etc. Second edition, thoroughly revised and enlarged. Cloth. Price, $15.00. Pp. 697, with 550 illustrations and 3 colored plates. Lea & Febiger, Washington Square, Philadelphia 6, Pennsylvania, 1951.

This comprehensive volume provides an excellent description of the many tumors which involve the skin and is unusual in that more than half of its 550 pages are devoted to a review of benign tumors and other lesions which might be confused with malignant cutaneous diseases. The remainder of the book covers the diagnosis and treatment of malignant tumors of the skin and special sections are devoted to carcinomas of the lip, mouth, penis and vulva sarcomas, melanomas and lymphoblastomas.

Various methods of treatment are given for each lesion but radiation therapy is stressed and roentgen-ray techniques utilizing the many voltages from the grenz-ray range up to 200 kv. are described. Radioactive materials are discussed but most of the radium therapy is carried out with contact applicators. A brief chapter on radiation physics includes a description of the Manchester System of radium dosage calculation and all radium dosages are expressed in roentgens. Although many accepted techniques are omitted from the text, a very complete bibliography is placed at the end of each chapter. Illustrations of good quality are used freely throughout the book.

The authors show a strong preference for surgical procedures in the care of large carcinomas and the advantages of low intensity radium needles receive scant consideration. Radiation therapy is not recommended for the care of metastatic cervical lymph nodes except in inoperable cases where only palliation is attempted. In the reviewer's opinion the greatest defect in this excellent book is one observed in many American publications; namely, the omission of carefully compiled statistics covering the results obtained with each method of treatment recommended.

CHARLES L. MARTIN, M.D.

TUMORS OF THE EYE. By Algernon B. Reese, M.D., D.Sc. (Hon.), F.A.C.S., Attending Ophthalmologist and Pathologist, Institute of Ophthalmology, Presbyterian Hospital, New York; Ophthalmologist to Memorial Center for Cancer and Allied Diseases, New York; Clinical Professor of Ophthalmology, College of Physicians and Surgeons, Columbia University. Cloth. Price, $20.00. Pp. 574, with 283 illustrations. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 49 East 33rd Street, New York 16, New York, 1951.

This medical classic furnishes in easy but compelling style the first complete summation

and evaluation of the modern knowledge of ocular neoplasms since Lagrange's book published in 1901.

Reese has worked as the ophthalmic consultant with the Memorial Center for Cancer and Allied Diseases for twenty-two years, and besides an extensive private practice, he has a large service at the Institute of Ophthalmology of the Columbia-Presbyterian Medical Center.

The book begins with an exhaustive consideration of typical epithelial tumors of the lid, with original photographs and drawings and with surgical diagrams of the methods of removal.

The book proceeds with epithelial tumors of the uvea, and then with a section on retinoblastoma. This is one of the eye tumor subjects on which Reese is a well recognized international authority. Not only has he written the full details of management by means of surgery and irradiation but the facts of heredity are assembled for practical use.

Glioma is differentiated from retinoblastoma as a astrocytoma of the eye and its treatment along with that of similar conditions, such as tuberous sclerosis, is given. Orbital tumors are considered. This section is followed by chapters on tumors of the peripheral nerves, pigmented tumors and angiomatous tumors; finally the rarer eye tumors, such as leiomyomas, rhabdomyomas, mixed tumors, dermoid cysts and neoplastic metastases to the eye and orbit are considered.

This original book was written without haste, and of great interest in it are the follow-up studies of patients for periods of ten to fifteen years and more.

Radiologists, ophthalmologists and physicians who devote themselves exclusively to tumors will consider this a standard reference for many years to come.

Alston Callahan, M.D.

The Treasury of Human Inheritance. Edited by L. S. Penrose, M.D., Galton Laboratory, University College, London. Volume V. On Hereditary Digital Anomalies. Part I. On Brachydactyly and Symphalangism. By Julia Bell, M.A., F.R.C.P. Paper. Price, $3.00. Pp. 31, with numerous illustrations. Cambridge University Press, American Branch, 32 East 57th Street, New York 22, New York, 1951.

This volume, part of an extensive treatise on human genetics, presents an excellent series of descriptions and pedigree plates of 124 cases of two (occasionally coexistent) hereditary digital anomalies published in the literature between 1808 and 1948. One hundred and thirty-one references are listed.

In teratological nomenclature, etymological definitions are preferable to limitations of terms to specific clinicogenetic syndromes. Hence, brachydactylia is regarded as any digital shortening, phalangeal or metacarpal (metatarsal). Inconsistently, however, symphalangia is limited in this monograph to "fusion" across only the proximal interphalangeal joint. Brachydactyly is classified into five main groups, lettered A to E. Briefly, type A is a brachymesophalangia, affecting all the digits (subgroup A1), including the proximal phalanx of the thumb; or the 2nd (A2) or 5th (A_3) fingers only. In B (commonly called apical dystrophy) the middle and distal phalanges of the 2nd to 5th digits are affected. C is a complex alteration of the proximal and middle phalanges, chiefly of the 2nd and 3rd fingers. D is a pollical brachytelophalangia. E is a brachymetacarpia.

A welcome restraint (long overdue in clinical literature) is exercised in discussing (p. 9) the relations between teratology and evolutionary speculation. The probable main cause of brachydactyly is considered to be premature ossification of the epiphyseal plate; in type A this accounts also for the commonly associated dwarfism. It seems to the reviewer that the not uncommon association of carpal or tarsal "fusions" with symphalangism, as in Kirmisson's (1898) case, should have been stressed, since it shows the presence of a general aberration of joint development. This association is also brought out in the cases of Freud and Slobody (1943) and Steinberg and Reynolds (1948), whose papers are listed. Incidentally, the time of origin of such "fusions" is unknown, but they may arise as an absence of joint cavitation at a cartilaginous embryonic stage (the regular existence of chondrified articular interzones in the normal synovial joints of the human embryo is no longer accepted, however). The roentgenologist should keep in mind that minor aberrations tending towards symphalangism may be either missed (*e.g.*, joint narrowing) or undetectable (*e.g.*, stiffness) roentgenographically.

This volume will serve to emphasize the opportunities afforded to roentgenologists to secure further data on anomalies, in regard to their heredity and their progressive ossification.

Although the general discussion of the anomalies is somewhat cursory, apparently the purpose of the book is to provide a compilation of the relevant data available on teratological genetics, and in this regard the work can be thoroughly recommended. These monographs will be treasured by all who are interested in human inheritance.

RONAN O'RAHILLY

BOOKS RECEIVED

LEHRBUCH DER RÖNTGENDIAGNOSTIK. Von H. R. Schinz, W. E. Baensch, E. Friedl and E. Uehlinger nebst Beiträgen von E. Brandenberger, A. Brunner. U. Cocchi, N. P. G. Edling, J. Eggert, F. K. Fischer, M. Holzmann, H. Krayenbühl, Å. Lindbom, E. Lindgren, G. A. Preiss, S. Welin, A. Zuppinger. Fünfte, völlig neu bearbeitete und vermehrte Auflage. 5. Lieferung. Innere Organe. Paper. Price, DM 84.-. Pp. 436, with 522 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1951.

LEHRBUCH DER RÖNTGENDIAGNOSTIK. Von H. R. Schinz, W. E. Baensch, E. Friedl and E. Uehlinger nebst Beiträgen von E. Brandenberger, A. Brunner, U. Cocchi, N. P. G. Edling, J. Eggert, F. K. Fischer, M. Holzmann, H. Krayenbühl, Å. Lindbom, E. Lindgren, G. A. Preiss, S. Welin, A. Zuppinger. Fünfte, völlig neu bearbeitete und vermehrte Auflage. 6. Lieferung. Innere Organe. Paper. Price, DM 98.-. Pp. 528, with 507 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

DIE NEUZEITLICHEN BRUSTWAND- UND EXTREMITÄTEN-ABLEITUNGEN IN DER PRAXIS. Von Prof. Dr. Herbert Reindell, Oberarzt der Medizinischen Universitätsklinik Freiburg i. Br., und Dr. Helmuth Klepzig, Assistent der Medizinischen Universitätsklinik Freiburg i. Br. Mit einen Vorwort von Prof. Dr. Ludwig Heilmeyer, Direktor der Medizinischen Universitätsklinik Freiburg i. Br. Cloth. Price, DM 22.50. Pp. 179, with 64 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1951.

VERLETZUNGEN DER LUNGEN UND DES BRUSTKORBES. Frühverlauf und Spätfolgen mit besonderer Berücksichtigung der Lungentuberkulose. Kritische Beobachtungen über 3 Jahrzehnte an fast 4000 Verletzten des Weltkrieges 1914/1918. Von Dr. Walter Steffens, Oberregierungsmedizinalrat i.R. ehemals Chefarzt der Versorgungsärztlichen Untersuchungsstelle Berlin. Paper. Price, DM 10.90. Pp. 319, with 45 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1951.

NOUVELLES TECHNIQUES OPÉRATOIRES DANS LA CHIRURGIE DU CANCER. Par Antonio Prudente, Professeur à la "Escola Paulista de Medicina," etc.; et Henrique Melega, Professeur agrégé à la "Escola Paulista de Medicina," etc. Paper. Price, 2,500 fr. Pp. 295, with 180 illustrations. Masson et Cie., 120, boulevard Saint-Germain, Paris 6, France, 1951.

DIE GENERALISIERTEN TUBERKULOSEN. Von Dr. med. F. Schmid, Heidelberg. Paper. Price, DM 24.-. Pp. 230, with 51 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1951.

KYMOGRAPHISCHE RÖNTGENDIAGNOSTIK. Zur Beurteilung des Herzens in Beispielen. Von Professor Dr. Pleikart Stumpf, München. Paper. Price, DM 25.50. Pp. 120, with 164 illustrations, Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1951.

ROENTGENOLOGIC DIAGNOSIS OF DISEASES OF BONES. By David G. Pugh, Assistant Professor of Radiology, Mayo Foundation, Graduate School, University of Minnesota; Consultant, Section on Roentgenology, the Mayo Clinic. Cloth. Pp. 316, with 307 illustrations. Thomas Nelson & Sons, 19 East 47th Street, New York, New York, 1950, 1951.

DIE GESUNDE UND KRANKE WIRBELSÄULE IN RÖNTGENBILD UND KLINIK. Pathologisch-anatomische Untersuchungen. Von Geh. Med.-Rat Prof. Dr. med. et Dr. med. vet. h.c. Georg Schmorl (†1932) für Röntgenkunde und Klinik bearbeitet von Prof. Dr. med. habil. Herbert Junghanns, Oldenburg (Oldb.). Zweite, wesentlich erweiterte Auflage. Cloth. Price, DM 69.-. Pp. 284, with 399 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1951.

PEPTIC ULCER. Clinical Aspects, Diagnosis, Management. By David J. Sandweiss, M.D., F.A.C.P., Editor, Associate Attending Physician, Division of Internal Medicine, Harper Hospital, Detroit, Michigan. Editorial Committee: A. H. Aaron, Henry L. Bockus, George E. Daniels, George B. Eusterman, L. Kraeer Ferguson, A. C. Ivy, Sara M. Jordan, Frank H. Lahey, Walter L. Palmer, Harry Shay, Albert M. Snell, and Dwight L. Wilbur. Cloth. Price, $15.00. Pp. 790, with 164 illustrations. W. B. Saunders Company, West

Washington Square, Philadelphia 5, Pennsylvania, 1951.

Renal Pelvis and Ureter. By Peter A. Narath, M.D., F.I.C.S., Adjunct Professor of Urology, New York Polyclinic Medical School and Hospital. Cloth. Price, $12.50. Pp. 429, with 264 illustrations. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, New York, 1951.

Geschwülste des Ohres und des Kleinhirnbrückenwinkels. Von Dr. med. K. Graf, Priv.-Doz. für Ohren-Nasen-Halsheilkunde an der Universität Zürich. Cloth. Price, DM 43.-. Pp. 283, with 132 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Diagnosis and Treatment of Menstrual Disorders and Sterility. By Charles Mazer, M.D., F.A.C.S., Formerly Associate Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania; Attending Gynecologist, St. Agnes Hospital; Consulting Gynecologist, Mount Sinai Hospital, Philadelphia; and S. Leon Israel, M.D., F.A.C.S., Assistant Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania; Attending Gynecologist, Mount Sinai Hospital, Philadelphia. Third edition, revised. Cloth. Price, $10.00. Pp. 583, with 115 illustrations. Paul B. Hoeber, Inc., 49 East 33rd Street, New York 16, New York, 1951.

Grundlagen der Strahlentherapie. Physik, Biologie und allgemeine Therapie. Von Dr. med. Richard Kurt Kepp, apl. Professor für Geburtshilfe und Frauenheilkunde an der Universität Göttingen. Mit einem Geleitwort von Prof. Dr. Heinrich Martius, Direktor der Universitäts-Frauenklinik Göttingen. Cloth. Price, DM 38.-. Pp. 357, with 134 illustrations. Georg Thieme, Diemershaldenstrasse, 47, Stuttgart, Germany (Grune & Stratton, Inc., New York, New York), 1952.

Control and Removal of Radioactive Contamination in Laboratories. National Bureau of Standards Handbook 48. Issued December 15, 1951. Paper. Price, 15 cents. Pp. 24. For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

Proceedings of the First Conference on Electrokymography. Held May 25–26, 1950, in Bethesda, Md., sponsored by the National Heart Institute. Paper. Price, 75 cents. Pp. 215, with numerous illustrations. Superintendent of Documents, United States Printing Office, Washington 25, D. C., 1951.

Queensland Radium Institute. Seventh Annual Report to the Honourable the Minister for Health and Home Affairs. For the Year Ended 30th June, 1951. Presented to Parliament and Ordered to be Printed. Paper. Pp. 20. A. H. Tucker, Government Printer, Brisbane, Queensland, 1951.

Environment and Health. Federal Security Agency, Public Health Service, 1951. Paper. Price, 75 cents. Pp. 152, with numerous illustrations. Superintendent of Documents, Government Printing Office, Washington 25, D. C., 1951.

Annual Report. 1950 Professional Services. Paper. Pp. 145. Veterans Administration Hospital, 130 West Kingsbridge Road, Bronx 68, New York.

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ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Usinger, F. Zur Frage der posttraumatischen Spaltbildungen am Schädel. (Posttraumatic cleft formation in the skull.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Dec., 1951, *75*, 712–717.

This is a case report describing development of a finger-long and finger-wide cleft in a parietal bone of a two and a half year old child, thirteen months after a fracture of the frontal bone, at which time the parietal bone appeared normal, and in which the fractured frontal bone healed normally. The probable mechanism is that of a cerebral scar, in close relation to the ventricle, producing irritation and increased secretion of cerebrospinal fluid. The increased intracranial pressure forces the scar tissue out through a traumatic rent in the dura, between the edges of bone thus, preventing bony bridging.

Various clinical findings, in this case, and others from literature are: palpable pulsation, epilepsy, mental disturbance, ventricular widening, skull defects with herniation of brain, and meningocele spuria traumatica.—*John J. B. Light, M.D.*

Moore, Sherwood, and Carr, Archie D. Hyperostosis frontalis interna; two contrasting cases. *J.A.M.A.*, Jan. 19, 1952, *148*, 199–200.

The authors assume that the reader is familiar with the salient features of hyperostosis frontalis interna and do not go into discussion of the condition or its accompanying symptom complex. They report 2 strongly contrasting cases of this disease, one in a thin twenty-two year old white woman and the other in an enormously obese fifty-five year old negro woman. They point out that the first case refutes the opinion that this is a physiological process incident to menopause as does the fact that the condition rarely may be found in the male. The older of the 2 patients was first thought to have a pituitary obesity. After a period of three years, a readily demonstrable hyperostotic change in the skull developed.

The first patient had been under observation for an unusually long time, and progressive changes were found to occur in the vault of the skull, which almost doubled in thickness and manifested a combination of hyperostosis frontalis interna and hyperostosis calvariae diffusa. Later there was regression of the thickening of the orbital plate of the frontal bone until it was normal in thickness. These phenomena were difficult to explain. No other regressive changes of similar nature have been found elsewhere in the skull in some 700 varying cases of hyperostosis.

There were certain common features in the 2 patients. Both were chronic invalids who suffered from intense headaches and had demonstrable abnormal changes in the skull, which were progressive in character. Neither patient had a male type of hair growth.

They conclude that hyperostosis frontalis interna is frequently baffling in the inconstancy of the signs and symptoms and requires an extended period of observation to establish an accurate diagnosis. They point out that the condition is never fatal, but the outlook for the unfortunate subject is at best mild invalidism, at worst psychosis.—*R. D. Moreton, M.D.*

David, M., Fischgold, H., Lairy-Bounes, G.-C., and Talairach, J. Diagnostic des gliomas par l'Eeg et l'angiographie conjuguées. (Diagnosis of gliomas by means of combined electroencephalography and angiography.) *Presse méd.*, Jan. 23, 1952, *60*, 81–84.

Electroencephalography associated with angiography give sufficient information to enable a positive diagnosis and localization of supratentorial tumors, hence often avoiding the necessity of ventriculography. Additional advantages are better evaluation of circulatory patterns of the tumor and of the brain and of the extent of edema, thus permitting a more precise prognosis. However, ventriculography remains of prime importance in the localization of the intra- and subventricular tumors. Clinical and electroencephalographic studies combined with roentgenographic study of the sella turcica help to determine the choice between angiography and ventriculography.

Direct signs of electroencephalography are indicative of superficial tumor of an approximate topography, whereas indirect signs may be due to a deeper tumor or to generalized edema of the brain and cranial hypertension. In supratentorial gliomas the most direct electroencephalographic sign (monopolar method) is an electrical silence indicative of a cortical tumor mass which is itself electrically inactive. A delta polymorphic rhythm is also registered. The indirect signs are the monomorphic rhythm suggestive of subcortical deeper tumors and the abolition of arrest reaction indicative of involvement of the regions of the great vein of Galen, internal cerebral veins and the periventricular areas.

Direct signs of angiography may help to localize a superficial as well as a deep-seated brain tumor whereas the indirect signs indicate modifications in the general configuration of a group of vessels at a certain distance from the neoplastic mass. In case of glioma, for example, the direct signs are a limited displacement of an artery, opacification of the tumor or, on the contrary, appearance of an avascular zone corresponding to the tumor area, modification of the vascular pattern often due to formation of new vessels and arteriovenous fistulae (significant of glioblastoma, articularly of the angionecrotic type) and various venous patterns. As to the anterior cerebral artery, the direct signs are as follows:

The initial loop of the frontopolar artery disappears (the frontopolar sign is negative) the pericallosal and the callosomarginal branches, as well as the distal branches of the frontopolar artery, lose their tortuous configuration and become distended into a regularly curved contour because of the adjacent tumor mass. The indirect signs, on the contrary, consist of an increase in the tortuousity of all of these branches of the anterior cerebral artery because of a distant pressure due to a deeper tumor mass. However, certain gliomas may infiltrate the intervascular spaces and thus fail to displace the vessels. The angiographic signs of the deeper tumors are best visualized in the frontal view and they are as follows: opacification of the neoplastic mass, formation of new vessels, fistulae and arteriovenous lakes. These signs should be studied in precise relation to the median line, to the falx cerebri and to the base of the cranium. One handicap, however, is that these signs are not always shown.

The authors think that study of the phlebograms (taken at the fourth, fifth, and sixth seconds of angiography) combined with electroencephalographic studies will lead to further progress in the diagnosis and evaluation of deeper brain tumors.—*Jirair N. Sarian, M.D.*

Birrell, J. F. Chronic maxillary sinusitis in children. *Arch. Dis. Childhood*, Feb., 1952, *27*, 1–9.

Reports imply that 1 in every 4 or 5 children requiring removal of tonsils and adenoids also needs attention to the maxillary antra. That removal of the adenoids and tonsils will cure 80 percent of cases of chronic sinusitis lends support to the theory that the natural regression of lymphoid tissue in the nasopharynx about puberty may determine this limitation of infection in the sinuses.

Of 240 case records examined, 160 related to boys and 80 to girls, a ratio of boys to girls of 2:1. A preponderance of children in the six to eight year age group was found.

The following symptoms have been noted: nasal catarrh; nasal discharge or running nose; frequent colds; nasal obstruction or mouth breathing; persistent cough; bronchitis; bronchiectasis; headaches; asthma; discharging ears or deafness; laryngitis.

One hundred and forty-five double punctures were carried out. The right antrum alone was punctured 51 times, and the left on 47 occasions. Thus, in the 240 cases 382 punctures were done. The total number of antra in which pus was found was 36; the total number showing mucopus was 17; while a total of 329 antra gave a negative result. That is to say, 9.42 per cent of the antra contained pus, and 4.45 per cent yielded mucopus. Less than one-fifth of the cases suffering from ear trouble gave positive proof puncture findings. Five of 11 bronchiectatic patients had a positive puncture. The association between chronic sinus infection and bronchiectasis is well recognized.

The author's experience shows that no reliable evidence can be obtained from roentgenographic study. Positive and negative results have been found in patients whose roentgenograms showed complete antral opacity or gross mucosal thickening. The appearances are not as diagnostic as in adults. In children the results are confused by the growth of the antra which are often shallow, and by the lack of air entry, either due to enlarged turbinates, enlarged adenoids, secretion lying in the nose, or habitual mouth breathing. The confusion in assessing roentgenograms was apparent in the case of 2 children of the same age, both showing pus in the nose and both suffering from bronchiectasis, who has bilateral punctures performed on the same morning. The roentgenograms of one child revealed bilateral antral opacity; those of the other showed a moderate degree of mucosal thickening. The child with complete antral opacity had a bilateral negative puncture, while the other child, with mucosal thickening showed pus in each proof puncture.

The author believes that roentgenograms are of no use in determining the nature of mucosal changes in children.

Chronic maxillary sinusitis cannot be diagnosed with certainty by clinical findings, blood examination, erythrocyte sedimentation rate, roentgenography, or bacteriological results from proof puncture.

In order to avoid missing the few cases with evidence of infection in the antrum, every patient showing antral abnormality on roentgenographic examination must be proof punctured. Until a reliable diagnostic criterion is discovered, this wholesale puncturing of antra must be continued as the only means of establishing diagnosis.

The sinusitis in most children can be cured by antral wash-out, with or without the removal of tonsils and adenoids. Conservative measures advocated for the treatment of sinusitis include change of climate to the seaside, Proetz displacement and roentgen therapy. A liberal supply of vitamin A and antibiotics may be instilled into the antra through indwelling catheters.

Should conservatism fail, or minor surgery not result in a cure, recourse is had to antral surgery. The operation of current choice appears to be the Caldwell-Luc or radical antrostomy. Admittedly only a small percentage of cases require this operation.

The results of 382 proof punctures in 240 children, clinically and roentgenologically diagnosed as chronic sinusitis, showed positive results in 13.87 per cent, but only 2 children (0.53 per cent) were considered to be true cases of chronic maxillary sinusitis.

It is felt that the generally accepted theory that sinusitis is common in children is false, and does not

withstand critical examination. Identical clinical and roentgenological findings may be produced by habitual mouth breathing. Treatment should be directed in the first instance toward re-establishing nasal respiration rather than against a non-existent sinus infection.—*Stephen N. Tager, M.D.*

TERRAFRANCA, RAYMOND J., and ZELLIS, ALLAN. Rhinolith. *Radiology*, March, 1952, *58*, 405–407.

Rhinoliths may occur at almost any age but are especially frequent during the second and third decades of life. They are usually single and are found more commonly in females. The size varies greatly.

Two types are recognized: (1) exogenous (false) due to concretions about foreign bodies, and (2) endogenous (true) due to concretions laid down about a nidus such as blood clot, desquamated epithelium, and fragments of bone.

Symptoms may be of short duration even though the rhinolith may have been present for years. They include unilateral nasal discharge and obstruction, epistaxis, swelling of the nose and conjunctivitis.

Such conditions as syphilis, calcified polyps, osteoma, osteomyelitis and carcinoma should be considered in the differential diagnosis.

One instance of an elderly man in whom a rhinolith was found is reported.—*McClure Wilson, M.D.*

CASTELLANO, FRANCESCO; GUIDETTI, BENIAMINO; and OLIVECRONA, HERBERT. Pterional meningiomas "en plaque." *J. Neurosurg.*, March, 1952, *9*, *188–196*.

The authors summarize their experience in 15 verified and 10 clinical cases of pterional meningiomas "en plaque." There were 19 in women and 6 in men.

The duration of symptoms was, on an average, four years. In many cases the physical and roentgenographic examinations showed the alterations to be extremely advanced, indicating that the condition was of much longer duration.

Unilateral exophthalmos was the most frequent initial manifestation. Other patients complained of temporal swelling, headache, loss of vision and 4 cases showed mental impairment.

In 24 of the 25 cases roentgenographic studies made it possible to verify the diagnosis of sphenoidal meningioma "en plaque." The diagnosis was suspected clinically in the other cases and later was confirmed by re-study of the roentgenograms.

Encephalography and ventriculography were of little added value.

From the observations made during the follow-up study the authors conclude that surgery is not indicated unless relief is required of a specific complication. The tumors grow slowly and are extensive when first observed so that complete removal is, as a rule, not possible.—*Vernon L. Peterson, M.D.*

NECK AND CHEST

GOODMAN, HENRY I., and PARNES, IRVING H. Epiphrenic diverticula of the esophagus. *J. Thoracic Surg.*, Feb., 1952, *23*, 145–159.

An epiphrenic diverticulum is a pulsion or pressure diverticulum that is located just above the diaphragm. A distinction must be made between true epiphrenic diverticula and traction diverticula of the lower esophagus. Roentgenographically this differentiation should not be difficult. Approximately 65 per cent of the cases of epiphrenic diverticulum have an associated cardiospasm.

Epiphrenic diverticulum is not common. The authors found only 126 reported cases. The symptoms and indications for surgery are discussesd. The improvement in operative technique is reviewed. A new procedure, that of resecting the distal portion of the esophagus and cardia of the stomach with intrathroacic esophagogastrostomy, is described. Two patients are reported in whom this operative procedure was used.

The authors believe that the new operative procedure should be reserved for those cases which could not be adequately treated by diverticulectomy; namely, multiple diverticula, diverticula associated with cardiospasm, with esophageal atresia, or with neoplasm.—*Thomas C. Stansbury, M.D.*

MACARINI, N., and OLIVA, L. L'insufflazione del mediastino anteriore e posteriore per via precoccigea. (Insufflation of the anterior and posterior mediastinum by the precoccygeal route.) *Radiol. med.*, Feb., 1952, *38*, 105–118.

During the course of many retroperitoneal gas injections performed via the prococcygeal route for the direct visualization of the pancreas, the authors noted that the gas regularly diffused into the anterior and posterior mediastinum and into the neck. This observation induced them to try to increase the diffusion of the gas within the thorax so that the method could be used advantageously for the study of mediastinal lesions.

They proceed as follows: The gas is injected through precoccygeal puncture by following the technique of De Gennes, May and Simon, but the patient is placed in a ventral or right lateral oblique decubitus with the head and thorax much higher than the side of the puncture. After completion of the injection he is then made to lie for thirty minutes in ventral decubitus but again with the head and thorax much higher than the pelvis. Sometimes it may be necessary to let him stand up for a while and lean strongly forward or backward for a relatively greater diffusion of the gas into the posterior mediastinum or anterior mediastinum respectively as the case may be. The quantity of the gas injected is also important. The authors usually inject 1,400 cc. of

oxygen in the average individual of normal build. It appears that the optimal degree of mediastinal emphysema is reached within about one hour but some individual variation exists; in thin persons, for example, the oxygen diffuses more rapidly than in fat persons. Occasionally, an emphysema of the neck is also noted, as a rule, concomitantly with the appearance of the mediastinal emphysema. In a single case a dysphonia of temporary duration occurred.

The authors give a detailed description of the anatomical areolar spaces which make possible the diffusion of the gas from the precoccygeal area through the retroperitoneal tissues into the mediastinum and from there into the neck.

The constrast study includes conventional roentgenography and laminagraphy in frontal, sagittal and transverse axial planes. The authors strongly emphasize that an association of pneumomediastinum with laminagraphy is essential since the two methods complement each other. They reproduce laminagrams made in various planes and at various levels to illustrate this point.

The conclusion is drawn (1) that the method described is devoid of danger, since the precoccygeal space is from 1 to 3 cm. wide in the posteroanterior direction and contains no vessels facilitating embolism; (2) that it is easy to carry out technically; (3) that it has the sole inconvenicence that the rectum may be punctured, in which case the needle is withdrawn and the procedure is resumed the next day; (4) that it causes no untoward effects, the slight upper abdominal pain and the sensation of retrosternal pressure usually being relieved when the patient breathes superficially; and (5) that it permits simultaneous visualization of the anterior mediastinum and of the posterior mediastinum, as well as of the retroperitoneal spaces.

The various routes presently used for the injection of gas into the mediastinum may be divided into (1) direct, comprising the (a) retrosternal, (b) pretracheal and (c) transtracheal routes; and (2) indirect, comprising the (a) intraspinal extradural, (b) precoccygeal and (c) laterovertebral routes. The direct routes enable contrast visualization of only the anterior or posterior mediastinum into whichever the injection has been made, whereas the indirect routes always lead to simultaneous visualization of both mediastina.—*T. Leucutia. M.D.*

Ellis, F. Henry, Jr., Good, C. Allen, and Seybold, William D. Intrathoracic goiter. *Ann. Surg.*, Jan., 1952, *135*, 79–90.

The authors review 24 cases of intrathoracic goiter as an aid to establishing criteria for accurate preoperative diagnosis and proper operative treatment. These cases are from the Mayo Clinic.

Statistical figures are as follows: Age and sex—17 patients were women; the average age was 50.8 years; two-thirds were more than 50 years of age. Twelve patients had previous surgery; 3 had undergone surgery two times. Average duration of discovery of tumor after surgery was 10.2 years.

Symptoms: Only 12 patients had any symptoms and these were due to pressure from the tumor. Symptoms were dyspnea, cough, hemoptysis, pain, dysphagia and wheezing, weakness, etc. On physical examination only 10 patients had palpable thyroid glands. Six patients had bronchoscopy which revealed narrowing due to external pressure.

Laboratory studies showed an increase in basal metabolic rates to be present in 3 cases. Radioactive I^{131} was used in 2 cases, and in each case demonstrated the I^{131} to localize in the intrathroacic mass.

Roentgen study was done in all 24 cases with 23 available for review. Thirteen tumors were in the right portion of the superior mediastinum. Nine of the remaining 11 were in the anterior mediastinum, and 2 were in the posterior mediastinum in the region of the necks of the ribs and the thoracic vertebrae. Five of the 11 were on the right, 3 on the left, and 3 were bilateral. The 2 tumors in the posterior mediastinum proved to be metastatic lesions. Calcium was visible in 9 cases. In 6 the deposits were central, in 2 linear and in 1 in the superior pole. Tracheal deviation was demonstrated in 9 cases. In 11 of 19 cases, which were fluoroscoped, the masses had been seen to move during swallowing. Pulsation was seen in 2 cases. Some complications encountered were effusion in 1 case and paralysis of the diaphragm in 1 case. Only 7 of 24 cases were diagnosed preoperatively by the radiologist.

Other diagnoses made were dermoid, neurofibroma, lymphoblastoma, thymoma, bronchogenic cyst, teratoma, leiomyoma of esophagus, and echinococcus cyst. With the use of the clinical and roentgenological data, 14 cases were diagnosed correctly.

Pathologically all tumors presented as rounded or ovoid lobulated masses in the mediastimum. Microscopic examination revealed the typical picture of an adenomatous goiter with scattered degenerative and cystic areas, except for 1 case of adenocarcinoma.

Positions of the masses were as follows: 18 of 24 tumors were on the right; this is thought to be due to the fact that the aorta limits extension to the left. The authors state that although posterior mediastinal goiters have been considered rare, in 14 of their cases the lesion was located in the posterior mediastinum or the posterior portion of the superior mediastinum. The blood supply to these masses was usually found to arise from the inferior thyroid artery. They may also receive blood from the aorta, the subclavian and internal mammary, and intrathoracic arteries.

The authors feel that the intrathoracic masses entered the thorax from the neck, and later lost their connection with the parent gland; this does not include the metastatic lesions.

The postoperative complications were shock, paralysis of vocal cords, thrombophlebitis, atelectasis, and empyema.

Throughout the article many excellent roentgenograms are presented showing very bizarre configurations for intrathoracic thyroid, and one can readily understand the difficulty of the problem of differential diagnosis on the basis of roentgen study alone. The authors list their criteria for the roentgenological diagnosis, of which the most important is the combination of displacement of the trachea with an upward motion, evident on swallowing.

An evaluation of treatment is given. This they feel depends on the individual case. Removal of the tumors is advisable because of the threat of hyperthyroidism, malignant change and of mechanical interference with the airway. They discuss the problem of surgery as to the tumor side, and a classification of operations is given, varying from the routine cervical approach to a sternal-splitting operation.—*L. L. Lemak, M.D.*

ANDERSON, ROBERT J. Review of mass chest x-ray surveys. *J.A.M.A.*, Feb. 23, 1952, *148*, 605–608.

The author reports some aspects of the value of 14 community wide chest surveys with small film screening of nearly 5½ million persons from all parts of the country.

Muscogee County, Georgia, was selected as the over-all chest plot base for studying the effects of mass surveys and correlation with tuberculin sensitivity findings and general tuberculosis mortality information. It is apparent that the immediate effects of a chest roengten-ray survey may depend on the importance of endogenous disease that becomes active after the screening program.

In the three and a half years since the initial program, the average annual death rates for tuberculosis appear to be about the same for the groups receiving roentgen examination and for the groups that did not. Without screening, however, because of prompt isolation and treatment the death rates of surveyed groups would perhaps have been higher.

There were 25 post survey deaths among persons whose survey roentgenograms were free of evidence of tuberculous infection. Three were whites and 22 were negroes. It would appear that resurveys in the more susceptible groups should be made at more frequent intervals.

The first stage of the survey operation—that is, the small film screening examination of 80 per cent of the eligible population in each community fifteen years of age or over, has varied from 55 to 93 per cent.

The second stage of the survey operation—confirmation by 14 by 17 inch films for suspicious small film findings has varied from 2-7 per cent of the number of small film examinations. Between 80 and 95 per cent of those recalled have responded.

Of the total number of 14 by 17 inch film examinations, the total prevalence of findings suspicious of tuberculosis has been from 0.6 to 2 per cent of all persons receiving small film examinations. The rate is higher in the lower economic levels.

The question of how much active tuberculosis is found is fundamental. One of every 1,000 screened persons will have active tuberculosis, clinically recognizable. In addition, many of those found with inactive or questionably active disease will later prove to be active; 85-90 per cent of these cases are unknown to the health department.

The importance of finding other pathological conditions in the chest, usually silent, is stressed, particularly in the older age groups. This applies especially to neoplasms and cardiovascular abnormalities.

The community surveys stimulated many areas to improve their tuberculosis control programs. More knowledge was gained and public interest was aroused in tuberculosis control and care.—*Norman Heilbrun, M.D.*

MCKINNON, N. E. Cancer mortality; the failure of control through case-finding programs (a summary). *Surg., Gynec. & Obst.*, Feb., 1952, *94*, 173–178.

Cancer case-finding programs were organized for the purpose of materially reducing cancer mortality. Wide variety in those programs has provided an unintentionally controlled experience over the past twenty to thirty years.

The age specific rates of breast cancer mortality do not show any decline or any change in their trends or any difference between trends but have consistently maintained fair levels regardless of the presence or absence of case-finding programs or their varying effectiveness in bringing cases to attention. This experience, as it has been recorded in vital statistics, clashes with the faith in early treatment upon which control programs were based.

Examination of representative evidence generally advanced and accepted as supporting that faith fails to show any in which due allowance was made for the natural history of the disease, for different lethal types and for present inability to differentiate between those types. Further, as staging is more a classification of type than of time and Stage I includes cases of short and long duration, results in Stage I cases are not evidence of results of early treatment. Thus, none of the evidence with purports to show that early (or different) treatment prevents death (or prolongs life) in breast cancer is sound evidence.

On the other hand, direct evidence from analysis of cases indicates that type of breast cancer rather than time or type of treatment determines the outcome and, in fatal cases, its time. Even the data advanced as supporting the faith in early (or different) treatment can be consistently interpreted as indicating natural selection by different types of cancer.

These findings in regard to breast cancer—the

failure of early treatment to reduce recorded mortality, the fallibility of the evidence for faith in early treatment, the dependence of the outcome on the type of cancer rather than on time or type of treatment, the present inability to differentiate between different lethal types and the lack of correlation between stage and duration—are applicable in general to other metastasizing cancers. In those that, untreated, usually cause death by local extension before remote metastases become manifest, treatment can prolong life; in nonmetastasizing cancer (indistinguishable morphologically from metastasizing cancer) treatment can cure. But in both these forms of cancer in which treatment provides more than mental and physical relief, treatment within a reasonable time after the first indications of a lesion gives practically the same results as earlier treatment. Any attempt to reach these cancers in a very early stage carries with it a potentiality for much harm and but little good. Moreover, nonmetastasizing cancer contributes only a very small part of cancer mortality.

For the vast majority of cancer deaths, the evidence shows that the high claims of propaganda have not been substantiated nor have the high hopes of control been realized. The failure of early treatment to reduce mortality shows that spread of remote metastases occurs before interference is possible.

It must be concluded that case-finding and control grams have not accomplished and cannot, today, accomplish the purpose for which they were established, that they do not represent a sound investment from the point of view of return for the money involved and that they do not spell progress for public health.—*Mary Frances Vastine, M.D.*

Salzman, Emanuel, Peck, Mordant E., and Neerken, A. J. Methocel-diodrast: a viscous water-soluble contrast medium for bronchography; roentgen and clinical results in 23 cases. *Radiology*, Feb., 1952, *58*, 209–214.

This is a preliminary study of a mixture of diodrast and methylcellulose as a contrast medium for bronchography. The authors give a brief review of other contrast media that have been used, with comments on their advantages and disadvantages.

Methocel-diodrast is an aqueous solution of 50 per cent diodrast and 1.75 per cent methylcellulose of approximately the same viscosity (4,000 cps.) as the iodized oils. Methylcellulose given intravenously in many times the amount used in bronchography is retained by the reticulo-endothelial system. Evidence indicates the substance is excreted by the kidneys and the intestinal and bronchial mucosa. Studies on dogs showed transient foci of atelectasis and bronchopneumonia following methocel-diodrast mixture, but not as high an incidence as with iodized oil bronchography. These studies showed the diodrast to be rapidly absorbed from the lungs and excreted by the kidneys.

The authors routinely skin test (intradermal) patients with 0.1 cc. of 35 per cent diodrast before examination to learn of possible sensitivity. Their patients are prepared with atropine gr. 1/150 forty-five minutes before the examination and 50 to 100 mg. of seconal intravenously five to ten minutes before the examination. The pharynx, larynx, trachea, and bronchi are thoroughly anesthetized with 5 per cent cocaine; 15 cc. of methocel-diodrast is injected through a catheter resting on the carina and the solution is directed to one lung field, postero-anterior and lateral roentgenograms being made on one side before the other is injected.

The bronchial shadows are sharp for about four minutes, then absorption blurs their outlines. Normal lungs are clear of contrast medium one hour after completion of the bronchogram. Pulmonary disease causes a slight delay in absorption. One hour after the bronchogram a flat film of the abdomen generally shows the urinary tract irregularly outlined with diodrast.

Methocel-diodrast gives bronchograms of good quality, with good mucosal relief patterns. It mixes with the bronchial secretions readily, outlining bronchi partially filled with secretions. Mild febrile reactions (100-101° F.) occurred in 9 cases and lasted one day. One patient had a pneumonia lasting for eight days. In 2 patients with active tuberculosis, follow-up examinations five and six months later failed to show spread of disease. One patient died, and cause of death was attributed to cocaine sensitivity (this occurred after the paper was submitted for publication and in a series of more than 50 patients).—*Dean Nichols, M.D.*

Löhr, Berthold. Vorbereitung zur Bronchographie und die lokale Anästhesie des Bronchialbaumes; unter besonderer Berücksichtigung der Impletol-Prämedikation. (Preparation for bronchography and local anesthesia of the bronchial tree; with special emphasis on impletol premedication.) *Chirurg*, Feb., 1952, *23*, 49–52.

The psychological preparation of the patient is an important factor in bronchographic procedure. Cooperation of the patient is improved if the purpose and nature of the examination are slowly and carefully explained to him in advance. No prior sedation is given except in cases of hyperthyroidism or cerebral pathology. The patient is seated comfortably in a chair and is permitted to pull on his tongue while a fine spray of pantocain solution is applied to the base of the tongue and posterior pharyngeal wall. The solution consists of one per cent pantocain to which 20 drops of adrenalin (1:100) are added to reduce resorption of the pantocain. It is advisable to remind the patient repeatedly that his respiration

remains good. A few drops are placed on the epiglottis and flow down to the cords, another drop is placed directly on the cords, then 1-3 drops directly on the trachea for a total of 1.5 cc. The patient bends toward the affected side for the last 0.5-0.75 cc. To avoid aspiration of vomitus, the patient is requested not to eat on the day of the examination. Excessive secretion or signs of infection demand postponement of the study since a differential diagnosis between small neoplasms and mucous plugs may be quite difficult.

In 230 bronchographic examinations, only 1 patient required a general anesthetic for psychic reasons. A good local anesthetic suffices for a proper investigation of the anatomical and physiological status of the bronchial tree. Reduction of secretion and depression of the vagovagal reflex are obtained by the subcutaneous injection of 1.0 cc. atropine one-half hour prior to the procedure. At this time, the patient also receives an intravenous injection of impletol (a combination of novocain and caffeine). Novocain depresses the sympathetic nervous system without affecting the psyche, thus reduces bronchial spasm, salivation, perspiration, nausea, muscle tremors, and pain. Novocain also prevents atelectasis and may even release existing atelectasis. Caffeine not only reduces the toxicity of novocain but potentiates its desired effects. Local anesthesia assures cooperation of the patient during the entire procedure so that full respiratory excursions may be studied fluoroscopically and coughing may be produced at will during or after the procedure. The patient is immediately ambulatory at the conclusion of the examination. A subsequent elevation of temperature is a rarity. Pantocain reactions are treated with pure oxygen or intravenous barbiturates, but these are infrequent since the total quantity used is 3.0 cc. or 30.0 mg. Reactions from such a small quantity of medication must be attributed to individual idiosyncrasy and are almost always reversible. The author has used 0.5-1.0 cc. impletol in 54 cases without complications.—*Joseph Zausner, M.D.*

Garland, L. H., Miller, E. R., Zwerling, H. B., Harkness, J. T., Hinshaw, H. C., Shipman, S. J., and Yerushalmy, J. Studies on the value of serial films in estimating the progress of pulmonary disease. *Radiology*, Feb., 1952, *58*, 161–177.

Serial roentgenograms, made at intervals of two to three months, commonly form an important factor in estimating the presence of change or activity in cases of chronic pulmonary disease. It is generally supposed that such series can be interpreted with a high degree of accuracy. This study is designed to investigate the validity of this assumption, by determining how consistent are the interpretations of two posteroanteroir roentgenograms of the chest, made three months apart, in a series of patients, by several examiners.

A series of 150 patients with established pulmonary tuberculosis was independently selected. A pair of standard 14 by 17 inch films, made three months apart, was chosen for each patient. The examiners were three radiologists and three chest specialists, each well recognized in his field. They were given no information except which was the first and which was the second film of each pair. Each individual interpreted each pair of films independently; and after an interval of several weeks, the interpretations were repeated without recourse to the initial readings. Thus, observation was made of each individual's consistency of interpretation (*intra*-individual consistency) as well as that of each reader with the other five readers (*inter*-individual consistency). By agreement, interpretations were reported as "better," "no change," or "worse," with further agreements as to the definitions of these terms. Since the changes in the right and left lungs were often disparate from each other, opinions were to be expressed: first, as to the chest as a whole; second and third, as to each of the lungs separately.

Neglecting, for the sake of brevity, much of the interesting discussion of the results, the important findings were:

1. In judging a serial pair of films as described above, two readers are likely to disagree with each other in nearly one-third of the cases. A single reader is likely to contradict himself in about one-fifth of the cases.

2. A relatively small but significant factor in this error results from variation in technical factors, *i.e.*, poor film quality; difference in exposure and/or development between the serial films.

3. A reader is almost as likely to disagree with himself or with another reader when the lesion is unilateral, as when it is bilateral; *i.e.*, film pairs with contradictory evidence presented by the two lungs were not a major reason for disagreements.

4. In reading the same pairs of films at different times, when the opinion is either "better" or "worse," the chances are that in about 10 per cent of the cases another reader will use the opposite classification; and the same reader is likely to reverse his own original opinion in about 7 per cent of the cases.

The major conclusion is that serial roentgenograms of the chest, while probably the most accurately qualitative diagnostic tool at our disposal, should not be given more weight than they deserve as related to other evidence which the clinician may obtain. Terminology and description need further study and clarification. Much care is necessary to obtain films of uniform quality. In many cases, additional views other than the routine posteroanterior should be used to obtain the fullest possible information.—*Lynne Taylor, M.D.*

Chaves, Aaron D., and Abeles, Hans. Disseminated nodular pulmonary infiltrations of an indeterminate nature in apparently healthy persons. *Am. Rev. Tuberc.*, Feb., 1952, *65*, 128–141.

A survey of the large volume of material available from 23 chest clinics and survey units of the Bureau of Tuberculosis, New York City Department of Health, uncovered disseminated nodular pulmonary infiltrations unaccompanied by lymphadenopathy in 75 apparently healthy persons. A clinical diagnosis could not be made in any one of these cases.

The clinical observations showed 45 males and 30 females; 56 white and 19 negro patients. All but 8 were life or long time residents of New York City. None was employed in a dusty industry; 62 were in the twenty-one to forty age group. Mean observation period was three to five years.

In 54 cases gastric content was stained and cultured for *M. tuberculosis*. In 21 cases stained smears alone were examined. All were negative. Tuberculin reactions were tested in 71 cases. Negative results were obtained in 40 cases and positive reactions in 31 cases.

Other skin tests were done in random cases. There were 2 positive histoplasmin reactions; 1 positive coccidioidin reaction in 14 persons tested for both antigens. Four persons had a positive serologic test for syphilis. There were 2 "sarcoid type of granulomas" in 4 biopsies.

The roentgen findings at discovery (there were 31 cases in which previous films were available) were classified as:

(1) Fine nodular infiltrations in 10 cases. Of these 6 subsequently regressed, 3 were stationary, 1 progressed.

(2) Medium size nodular infiltrations in 23 cases; 22 regressed, 1 remained stationary.

(3) Large nodular infiltrations in 10 cases; 8 regressed, 2 remained stationary.

(4) Mixed, nodular of any size with predominantly linear types of density in 32 cases; 20 regressed, 17 remained stationary, 5 showed progression. Regression may take up to sixty months; the average in complete cases was twelve months. In the 6 progressive cases 2 developed cor pulmonale; 1 died of right heart failure; the remaining 3 showed extensive pulmonary fibrosis and multiple bullae.

These cases indicate an entity which must be considered after disseminated tuberculosis, mycosis, sarcoidosis and pneumoconiosis have been ruled out. The high spontaneous remission rate and low slow progression rate is important in the correct management of these cases.—*Edward Julien, M.D.*

Ødegaard, Haakon. The roentgenological picture in chronic, non-specific fibrosis of the middle lobe, with special regard to the value of planigraphy. *Acta radiol.*, Jan., 1952, *37*, 17–27.

A brief account is given of 20 patients with chronic middle lobe fibrosis of nonspecific nature The author examined these patients in the Department of Roentgenology of the University Hospital, Oslo, Norway. There were 11 females and 9 males and they ranged in age from twenty-four to seventy years. Eleven were over fifty years of age. Six of these patients had previously suffered from pneumonia, 1 had had pleuritis and 1 had had tuberculous lung disease several years previously.

In 5 patients the disease was discovered accidentally (in 2 by mass photofluorography, and in 3 by other routine examinations of the chest). The remaining 15 patients came for examination on account of recurrent colds, bronchitic symptoms or persistent cough. Hemoptysis occurred in 10 cases. A further characteristic feature appeared to be that most of the patients were in good general condition and that often nothing pathologic was noted on physical examination of the chest.

Laminagraphy was employed in 18 cases, and in 6 of these cases, where bronchoscopy revealed distinct constriction of the middle lobe bronchus, manifestation of this was also found by laminagraphy. Moreover, in 7 cases a calcified lymph node was seen on the laminagrams close to the bronchus of the middle lobe. In 11 cases signs of bronchiectases were revealed by laminagraphy, and in 10 cases, in which bronchography was also performed, this finding was confirmed. Bronchiectases were discovered in 2 more cases by bronchographic examination.

Laminagraphy in the lateral view was particularly helpful in outlining the course and caliber of the middle lobe bronchus. In most of the cases (12 out of the 18) no constriction of the middle lobe bronchus was found. Therefore, there seems to be no reason for confining the term "middle lobe syndrome" only to those cases in which such constriction is demonstrated at the time of examination.—*Mary Frances Vastine, M.D.*

Slavin, Paul. Diffuse pulmonary granulomatosis in young women following exposure to beryllium compounds in the manufacture of radio tubes. *Am. Rev. Tuberc.*, Feb., 1952, *65*, 142–158.

Nine patients showing diffuse pulmonary ganulomatosis resulting from exposure to beryllium in the manufacture of radio tubes are discussed.

Each of these patients sought medical advice for cough, shortness of breath and weakness. Due to lack of fever and pain and lack of early distressing symptoms, all were far advanced cases when first seen.

The period of exposure varied from eighteen months to fourteen years; the average was about six years. Exposure was either to spray or dust in the preparation or the mounting of cathode or filaments in cathode tubes which are beryllium coated. In 2 cases a clear occupational history was not recorded.

The initial chest roentgenogram showed multiple nodular densities overshadowing both lungs fields. Small and giant bullae, hilar adenopathy and 4 cases of pneumothorax were seen.

Four cases came to autopsy. Consistent microscopic findings in all were fine noncaseating nodules, diffuse fibrosis and areas of emphysema.

From the present series of cases it appears that chronic pulmonary beryllium granulomatosis is a grave incurable disease.—*Edward Julien, M.D.*

ABELES, HANS, and CHAVES, AARON D. The significance of calcification in pulmonary coin lesions. *Radiology*, Feb., 1952, *58*, 199–203.

The authors report their experiences with 13 cases of calcifications in solitary circumscribed densities in the lung parenchyma (coin lesions). Five lesions and 1 in addendum were resected. Three of these were hamartomas and 3 tuberculomas. The remaining 8 lesions observed from two to twelve years did not change. All patients were asymptomatic and all but 1 were men. Though rare cases of bronchogenic carcinoma enveloping a tuberculoma and calcification in a sarcoma do occur, the demonstration of calcification within such a lesion is strong evidence for benignity. Surgery as a routine should be avoided in this circumstance, and an attempt should be made to detect calcification in all coin lesions, including the use of laminagraphy when available.—*William A. Goodrich, Jr., M.D.*

TROEN, PHILIP. Explosive outbreak of an atypical pneumonia ("K-8 fever"). *A.M.A. Arch. Int. Med.*, Feb., 1952, *89*, 258–269.

Forty-five cases of a disease characterized by hazy pneumonic patches, marked constitutional symptoms, and unknown etiology are reported. All were patients or staff members associated with a single ward in an Army hospital in Kobe, Japan. Thirty-three patients had onset of symptoms within a five day period, and the explosive nature of the disease is readily apparent.

Pulmonary involvement ranged from small patches to extensive hazy densities. It was bilateral in 34. One-third of the patients showed clearing on their chest roentgenograms within ten days, while one-fourth did not show complete clearing three to four weeks later. One patient developed pleural effusion.

Frequent clinical findings were stiffness of the neck, high temperature, a localized cutaneous eruption, splenic and hepatic enlargement. The course in several patients was prolonged by marked asthenia.

Normal white blood cell counts were the rule, with a later tendency to lymphocytosis and eosinophilia. The erythrocyte sedimentation rate was elevated as long as the pulmonary involvement persisted. A large percentage of abnormal cephalin-cholesterol flocculation was noted. Spinal fluid tests were normal.

All efforts to establish a diagnosis remained unsuccessful. Bacteriologic studies revealed no pathogenic microorganism. Attempts to isolate a virus or rickettsial agent failed. Serologic studies were negative.

Treatment by antibiotics was not effective. Twelve patients received no antibiotics, other groups were treated with aureomycin, penicillin, a combination of both, or choloramphenicol and other drugs. No variation was apparent in the course of the disease in the different groups.—*Arthur A. Brewer, M.D.*

POMERANTZ, HAROLD Z., and WASSERMAN, EDWARD. Chronic Friedlander's pneumonia. *Canad. M.A.J.*, Feb., 1952, *66*, 137–139.

Acute Friedländer's pneumonia may be complicated by chronic pulmonary sepsis, which results in bronchiectasis, lung abscesses, cavitation, and repeated bouts of pneumonia. It can be easily confused with tuberculosis, and should be considered in the differential diagnosis of every case of pulmonary cavitation. It also may be confused with coccidiomycosis and other chronic pulmonary diseases.

Four cases are reported in detail. Three were treated prior to availability of the newer antibiotics; under treatment with large doses of sulfadiazine each progressed to a chronic form of pulmonary sepsis. One progressed to death; one was improved and discharged with residual disease present and lost to follow-up. A third case had repeated bouts of pneumonia, and a persistent focus of infection in the left antrum. Penicillin and other measures failed to eradicate the organism. When streptomycin became available the patient was given a ten day course of aerosol streptomycin; subsequently, and for the first time, the organism could not be cultured from the left nostril, and the patient was discharged.

The fourth case did poorly on chloromycetin. When this was changed to streptomycetin he improved. Later sulfadiazine was given in addition. The sputum became negative after forty days of treatment, but roentgen examination revealed persistent cavitation in the right upper lobe. A lobectomy was performed. He has been well subsequently. —*Arthur A. Brewer, M.D.*

ROSSELLI, JULIO, BLANCO, CARLOS, and SABBIONE, RICARDO M. Las neumonitis por virus en la infancia. (Virus pneumonitis in infancy.) *Prensa méd. argent.*, Feb. 22, 1952, *39*, 321–334.

Virus pneumonitis whether of known etiology (grip, ornithosis, Q fever) or of unknown etiology (primary atypical pneumonia) shows similar manifestations from a clinical, roentgenological and therapeutic viewpoint. In infancy, as in other periods of life, it occurs sporadically or in epidemics. In one epidemic in which 51 cases were observed, 16 were found in nursing infants. There was frequently an

absence or a minimum of physical findings in the presence of extensive roentgen changes.

Roentgenologically the first manifestation of the disease begins in the region of the hilus. The disease then radiates fan like in linear infiltration toward the middle zones, most frequently in the lower portions of the lungs. Peripheral densities with secondary hilar involvement were found less frequently. Posteriorly the involvement appears as parenchymal infiltrates of various shapes and locations, usually at the bases. The shadows have characteristic, ill defined, hazy borders and are less dense than those found in a pneumococcic pneumonia and do not erase the linear markings. Rarely there is a disseminated diffuse involvement of both lungs and exceptionally there is a pleural effusion. Clearing of the lungs takes place in a period from one to three weeks in a centripetal pattern.

Sputum examination, cold agglutinins and streptococcic agglutinations were frequently necessary to exclude pneumococcic pneumonia and tuberculosis. In nursing infants, the symptoms of disease were severe, complications were found to be more frequent and the mortality was high (31 per cent). The sulfonamides, penicillin and streptomycin were ineffectual in treatment. Excellent results, however, were obtained with aureomycin, chloromycetin and terramycin.—*Murray M. Friedman, M.D.*

Seaman, William B., and Goldman, Alfred. Roentgen aspects of pulmonary arteriovenous fistula. *A.M.A. Arch. Int. Med.*, Jan. 1952, *89*, 70–81.

The clinical features of cyanosis and clubbed fingers, associated with polycythemia and pulmonary murmur, enable the aware physician to easily recognize the full blown clinical syndrome of pulmonary arteriovenous fistula. Many cases are associated with cutaneous and mucosal hemangiomas and telangiectasia, probably a variant of Rendu-Weber-Osler disease (hereditary capillary telangiectasia). With the study of more cases it has become apparent that one or more of the clinical findings may be absent and, in some cases, the roentgen appearance may be the only positive finding leading to the correct diagnosis. Since the lesion is surgically curable, its recognition is important.

The authors have studied 8 cases of pulmonary arteriovenous fistulas in the last ten years. A résumé of the clinical finding and an excellent evaluation of the roentgenographic techniques are given in this very informative paper.

The age distribution ranged from twenty-two to seventy-nine years and the sex incidence was evenly divided. In 50 per cent of this group there was an absence of clubbing, cyanosis and polycythemia, necessitating greater reliance on the roentgen examination for the recognition of the disease. Although pulmonary arteriovenous fistula occurs in only a small number of cases of Rendu-Weber-Osler disease, the presence of hereditary telangiectasia should suggest that possibility. Few cases have been reported in children, despite the fact that this is probably a congenital lesion.

The most important roentgen finding is a rounded or lobulated mass with smooth discrete margins. The mass is most commonly seen in the lower and right middle lobes and is connected to the hilus by two or more sinuous linear shadows which probably represent the afferent and efferent vessels. These vessels are usually larger than the surrounding pulmonary vessels and their course is more tortuous. The vascular character of the lesion may be brought out by the Valsalva and Müller maneuvers which are recommended routinely in the fluoroscopic examination of these cases. The pulsatile nature of the tumor was demonstrated in 2 cases, both fluoroscopically and by roentgen kymography. The heart is not usually enlarged (in contrast to the enlargement noted in arteriovenous fistulae involving the systemic circulation).

Laminagraphy establishes the direct relationship of the mass to the pulmonary vascular shadows. Angiography is the method of choice for proving the vascular character of the lesion for self-evident reasons. The authors feel that a definitive diagnosis can be made with conventional roentgenography and laminagraphy but that angiocardiography is warranted in every case in which surgical treatment is contemplated.

The differential diagnosis is usually not difficult but small lesions may resemble pulmonary metastases, primary lung tumors, benign cysts, tuberculomas or bronchiectatic cavities filled with secretions. More than 65 proved cases have appeared in the medical literature in the thirteen years since the first clinical diagnosis was made by Smith and Horton. In 60 per cent of the reported cases there have been multiple lesions.—*D. L. Rousseau, M.D.*

Jacobi, J., Loeweneck, M., and Northoff, F. Die Diagnostik und Therapie der kongenitalen Angio-Kardiopathien. (Diagnosis and therapy of congenital cardiovascular diseases.) *Deutsche med. Wchnschr.*, Feb. 15, 1952, *77*, 193–197; also Feb. 22, 1952, *77*, 232–237.

The etiological factors in congenital cardiovascular diseases considered by the authors are: (1) developmental defects; (2) virus infections, especially rubella; (3) fetal endocarditis; (4) vitamin A and B deficiency; (5) roentgen therapy to the pregnant mother.

The diseases or anomalies are classified as follows:

Group 1: No shunt between lesser and greater circulation; acyanotic. This includes: (1) isolated pulmonic stenosis; (2) coarctation of the aorta; (3) dextroposition of the aorta; (4) double aortic arch; (5) anomalous subclavian artery; (6) stenosis or insufficiency of the valves; (7) dextrocardia.

Group II comprises those with a shunt and is further subdivided into the acyanotic and the cyanotic types. In the former subgroup are: (1) isolated ventricular or auricular septal defects; (2) auricular septal defect with congenital or acquired mitral stenosis; (3) persistent ductus Botalli; (4) anomalous pulmonary veins emptying into the right ventricle or superior vena cava and usually associated with a ventricular defect. The cyanotic subgroup (morbus coeruleus) includes: (1) tetralogy of Fallot; (2) Eisenmenger's complex; (3) tricuspid atresia and auricular septal defect (or ventricular septal defect if the right ventricle is hypoplastic); (4) transposition of the great vessels with or without a persistent ductus or ventricular septal defect; truncus arteriosus communis persistens, usually associated with a large ventricular septal defect or an absence of the septum (or triloculare); (6) anomalous return of systemic veins into the left auricle.

The important diagnostic aids are:

1. Detailed history with special reference to onset of cyanosis. Early onset suggests tetralogy of Fallot; delayed onset may be due to myocardial insufficiency, persistent ductus, or some other anomaly with a superimposed infection.

2. Degree of cyanosis. Is it masked by anemia or exaggerated by polycythemia? Is the cyanosis due to peripheral stasis, myocardial damage, or anoxemia in high altitude?

3. Polycythemia.

4. Dyspnea, either circulatory or respiratory in origin.

5. Condition of the eyes, noting especially the presence of cyanotic conjunctivae and status of the retinal vessels (retinal hemorrhage and choked disc are rarely found).

6. Thoracic deformity, associated with hypertrophy of the right ventricle.

7. Blood pressure, in coarctation, is high in the arms and low in the legs. In stenosis of the vessels near their origin from the aorta, the blood pressure is low or absent in the arms and high in the legs.

8. Murmurs and palpable thrills. Absence of a murmur does not exclude a congenital or acquired anomaly. A to-and-fro murmur is typical of a persistent ductus, seldom heard in tetralogy, often found in Eisenmenger's complex, and only occasionally in auricular septal defect.

9. Clubbing of all digits occurs in tetralogy, tricuspid atresia, true or false truncus, transposition of the great vessels, pulmonary arteriovenous aneurysm, and Eisenmenger's complex. Clubbing and cyanosis of the toes with normal fingers occur in the infantile type of coarctation. Clubbing of the fingers with normal toes and mild or no cyanosis is often seen in pneumoconiosis.

10. Electrocardiogram, showing a marked right axis deviation, suggests a tetralogy or an isolated pulmonic stenosis; marked left axis deviation suggests tricuspid atresia. A complete block in children is due to acquired myocardial damage or septal defect. An anterior wall infarction in the newborn is almost pathognomonic of a left coronary artery arising from the pulmonary artery.

11. Roentgen examination, especially fluoroscopy, gives information concerning the vascularity of the lungs. Diminished vascularity is seen in isolated pulmonic stenosis and tetralogy, whereas increased vascularity occurs in Eisenmenger's complex, transposition of the great vessels, persistent ductus, and auricular septal defect. Marked cardiac enlargement with cyanosis occurs in transposition of the great vessels and truncus arteriosus; without cyanosis, cardiac enlargement suggests auricular septal defect, anomalous emptying of pulmonary veins into the right auricle. An enlarged heart is also seen in disturbance of glycogen metabolism, perimyocarditis, and anomalous left coronary artery. Esophagrams show indentation on the right side of the esophagus in cases of high dextroposition of the aorta.

12. Circulation time is always shortened in the presence of a right-to-left shunt. Ether, decholin, or fluorescein is used by the authors.

13. Cardiac catheterization is harmless and permits the next two studies.

14. Gas analysis of the blood gives information regarding the direction and size of the shunt as well as the degree of arterial saturation. Several samples from the same site are taken to insure correct results.

15. Intracardiac pressure readings are especially important in studying cases with a septal defect or persistent ductus. In pulmonic stenosis, the pressure in the pulmonary artery is much lower than in the right ventricle. If the pressure is very high in the right auricle, a septal defect between the auricles or an isolated pulmonic stenosis is present.

16. Angiocardiography, performed by conventional methods, is limited to four views taken in three seconds (dextrocardiogram, pulmonary phase, levocardiogram, and outflow phase). Children from two to four years of age, receive 15–25 cc. of contrast material (80 per cent perabrodil); patients from four to fourteen are given 40 to 60 cc.; a total of 60 cc. is never exceeded.

17. Thoracoscopy is omitted by the authors.

The anomalies amenable to surgery are:

1. Coarctation of the aorta. The authors state that 25 per cent of the patients have a normal life span, 25 per cent die of cardiac insufficiency or hypertension, 25 per cent die of bacterial endocarditis, and 25 per cent succumb to a ruptured aortic aneurysm. The optimal age is eight to twelve years. Younger individuals present no real urgency, their collateral circulation is inadequate, and the aorta is as yet too small. Since atheromatous changes occur early, the uppermost limit for surgery is thirty years of age. The operative mortality is approximately 10 per cent. The operation consists of excising the involved portion of the aorta, then anastomosing the aorta to itself or to the subclavian artery. If this is not feasible, material must be obtained from an artery bank.

2. Persistent ductus. The life expectancy is poor

since 50 per cent die before the age of thirty and 20 per cent before the age of forty due to cardiac insufficiency or subacute bacterial endocarditis. The optimal age for surgery is six to twenty-five years. Resection is preferable but often only ligation is feasible. After successful surgery, the pulmonary circulation becomes normal, any existing endocarditis is arrested, and the typical murmur disappears. In the presence of an associated pulmonic stenosis, the operation is absolutely contraindicated.

3. Tetralogy of Fallot. The optimal age for surgery is four to twelve years. The purpose of surgery is to increase the blood supply to the lungs. An anastomosis is made between the pulmonary artery and the descending aorta (Potts' technique) or the left subclavian artery (Blalock's method). After surgery, cyanosis and polycythemia are reduced or absent, the work capacity of the patient is improved, and clubbing of the digits disappears, usually within one year. Operative mortality varies from 12 to 42.5 per cent.

4. Isolated pulmonic stenosis.

5. Tricuspid atresia.

6. Underdeveloped right ventricle.

7. Transposition of the great vessels.

The combined operative mortality is 12 to 45 per cent. Surgery fails in older patients, whose heart cannot accommodate for the increased flow in the pulmonary circulation. Extreme dextroposition of the aorta represents a hazard to surgery. Cases with an inadequate vessel for anastomosis or those with well established collateral circulation between the thoracic wall and the surface of the lung invariably die after exploratory thoracotomy. Among the operative complications are: (1) dilated veins over the pleura, for rupture of these vessels renders hemostasis very difficult; (2) thrombosis, which occurs if the anastomosis between the lesser and greater circulation is too small.

The authors strongly recommend the following steps in preparing the patient for surgery: (1) prolonged preoperative rest to allow the patient to become familiar with the surroundings, the physicians, and attendant personnel; (2) start antibiotics two days prior to surgery; anticoagulants are not used; (3) continuous infusions; (4) curare by intubation for the first stage of anesthesia, then oxygen. After surgery, suction drainage is continued for two days; antibiotics are usually discontinued after four to five days; early ambulation is not advised; and an oxygen tent is unnecessary.—*Joseph Zausner, M.D.*

Bostock, M. I., and Morris, William. Heart disease and mass miniature radiography. *Canad. M.A.J.*, Feb., 1952, *66*, 126–127.

The authors demonstrate that additional investigation of abnormal cardiovascular silhouettes as revealed by mass photofluorographic surveys is worth while. In their group 137 cases were selected out of 18,643. It is emphasized that approval for recall came from the family physician to prevent unnecessary workups from known cardiac disease and to avoid any suggestion that a public service was attempting to encroach upon private practice.

Of these 137 cases 33 could not be traced; 14 were known cardiacs.

Ninety cases were seen and clinically evaluated. Of this group 32 had no demonstrable cardiac disease; 34 had arteriosclerotic or hypertensive heart disease with cardiac enlargment; 16 had valvular heart disease and 7 had congenital heart disease.

The authors urge that only definitely abnormal cardiac silhouettes on photofluorograms should be selected for follow up if the greatest benefit is to be obtained from these surveys.—*T. D. Allison, M.D.*

Campos, J. M. Cabello. Aneurisma artério-venoso, aorto-pulmonar. (Arteriovenous aortopulmonary aneurysm.) *An. paulist. de med. e cir.*, Oct., 1951, *62*, 243–250.

The author presents the case of a laborer, aged forty-one, whose roentgenogram showed a tumor-like shadow protruding from the upper mediastinum bilaterally. By means of angiocardiography it was possible to demonstrate that the shadow on the right of the midline was due to an aneurysm of the brachiocephalic trunk while the shadow on the left side was caused by an aneurysm of the posterior knee of the aortic arch communicating with the pulmonary artery. The ramifications of the pulmonary artery were still visualized on the final roentgenogram (10 seconds after injection of cilatrast). So far the roentgen diagnosis has not been confirmed pathologically or operatively. Clinically it may also be of importance that the Wassermann reaction was strongly positive.—*Ernst A. Schmidt, M.D.*

Brown, F. Norman. Single left superior vena cava, with aortic coarctation, in an adult; case report. *J. Thoracic Surg.*, Feb., 1952, *23*, 160–163.

This is a case report of a man who was found at autopsy to have a coarctation of the aorta in close anatomic relationship to a single left superior vena cava. The theories of the etiology of coarctation of the aorta are discussed. In this case the author speculates on what effect mechanical pressure might have had on initiating or augmenting the constrictive process in the aorta.

The author believes that in this case surgical treatment of the coarctation might well have been impossible because of the anomalous left vena cava.—*Thomas C. Stansbury, M.D.*

Sokolov, Raymond A. Coarctation of aorta with surgical correction at age forty; report of a case. *J.A.M.A.*, Feb. 23, 1952, *148*, 641–642.

Since rather severe arteriosclerotic changes usually

develop in persons who have had coarctation for a long time, it is felt that the surgical correction is a hazardous procedure. The author reports the second successful operation on a person over forty years of age. Although the intercostal arteries were quite rigid from atheromatous change, the resected segment of the aorta was entirely free of change.—*Norman Heilbrun, M.D.*

ELLIOTT, ROBERT V., and PECK, MORDANT E. Thrombotic occlusion of aorta as demonstrated by translumbar aortograms. *J.A.M.A.*, Feb. 9, 1952, *148*, 426–431.

The literature on aortic thrombosis is reviewed. The technique of translumbar aortographic examination is reported giving the procedure used in injecting the contrast medium into the abdominal aorta.

Four cases are presented in which this procedure showed the exact level of thrombosis, and aided in determining the operative care of the patients.

The authors feel the procedure does not carry any undue risk.—*Fay H. Squire, M.D.*

SLOBODKIN, MORRIS. Goitre plongeant (plunging goiter) associated with pharyngo-esophageal diverticulum. *Radiology*, March, 1952, *58*, 378–382.

A case of goitre plongeant, or plunging goiter, is reported and illustrated by roentgenograms showing the goiter in its intrathoracic and intracervical positions. It presented an additional novelty in that it was associated with a pharyngo-esophageal diverticulum.

The mechanics by which a thyroid adenoma descends into the superior mediastinum are described. —*Arno W. Sommer, M.D.*

CIAGLIA, P. Intrathoracic meningocele; excision, with three and one-half years follow-up. *J. Thoracic Surg.*, March, 1952, *23*, 283–292.

The diagnosis of intrathoracic meningocele can be easily made, if the condition is kept in mind. The roentgen picture is that of a tumor in the posterior mediastinum. The usual preoperative diagnosis is neurofibroma, especially since intrathoracic meningocele is often associated with multiple neurofibromatosis. The correct diagnosis can be made by spinography or by needle puncture.

The author believes that intrathoracic meningocele is a progressive lesion and that, in general, surgery is indicated. The surgical indications and surgical treatment are reviewed and discussed.

A case of successful excision of an intrathoracic meningocele is presented. There has been no recurrance during a three and a half year follow-up.—*Thomas C. Stansbury, M.D.*

BENO, THOMAS J., and WEISEL, WILSON. Spontaneous contralateral pneumothorax complicating thoracic surgical procedures. *J. Thoracic Surg.*, March, 1952, *23*, 272–282.

Spontaneous contralateral pneumothorax complicating thoracic surgical procedures is extremely rare. Three cases are reported in this article and the few instances previously recorded in the literature are reviewed. The authors believe that the etiologic factor is most often a ruptured emphysematous bleb.

The awareness of this condition and the need for immediate diagnosis and treatment are necessary to avoid mortality. Clinical indications must suffice to warrant immediate thoracocentesis. Roentgen examination may cause the loss of valuable time and occasionally the patient's life.—*Thomas C. Stansbury, M.D.*

THOMAS, LOUIS B., and BOYDEN, EDWARD A. Agenesis of the right lung. *Surgery*, March, 1952, *31*, 429–435.

Three cases of pulmonary agenesis are presented. A two year old boy who had shown normal development and growth since birth was seen because of the aspiration of a foreign body. His chest was symmetrical and a roentgenogram showed collapse of right lung. Bronchoscopically a foreign body was seen in a bronchus leading off to the right. This bronchus was subsequently identified as a left middle bronchus. The foreign body was accidentally displaced into a bronchus leading to the left, subsequently seen to be the left lower lobe bronchus. The child stopped breathing at this stage and died. At necropsy, a right main stem bronchus was not found, and there was no pleural space on this side. The heart and other mediastinal structures largely filled the right portion of the thorax, and the left lung also partially filled this space.

In a second case, a sixteen day old twin girl was found to have agenesis of the right lung which was diagnosed roentgenographically. This was confirmed at necropsy, the child's death having followed an attempted repair of a tracheo-esophageal fistula. In this case also, a left middle lobe was present.

In a third case, that of a male infant who died one and a half hours after birth, it was found that the right lung was absent. No pleural space was found on the right side of the thorax. There was slight displacement of the mediastinum to the right. The right main bronchus was represented by a small nubbin on the trachea, at the normal site of bifurcation. A number of other developmental abnormalithe were present.

The authors point out that agenesis is most frequently misdiagnosed as atelectasis. They state that the most important physical features of agenesis are a symmetrical thorax, equal or nearly equal

respiratory movements and a marked displacement and rotation of the heart and mediastinum to the affected side.

The work of Wilson and Warkany is mentioned, these authors having found agenesis of the left lung in 5 rats subjected to maternal deficiency of vitamin A. The possible relationship between hereditary malformations and dietary deficiencies is discussed.

Schneider's classification is adhered to: (1) agenesis, that is, no development of bronchi or lung, (2) aplasia, that is, rudimentary bronchial development, but complete absence of surrounding lung tissue, and (3) hypoplasia, that is, rudimentary development of bronchial and lung elements. Boyden gives the anatomical analyses of the 3 cases.—*André Bruwer, M.D.*

Stender, H. St. Die Röntgensymptomatologie der Arteriitis pulmonalis und ihrer Folgezustände. (The roentgen symptomatology of pulmonary arteritis and its sequelae.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1952, *76*, 316–323.

The symptoms and course of pulmonary arteritis are described, which lead to the picture of primary pulmonary sclerosis. The history, clinical and roentgenologic, as well as the autopsy findings in 3 cases are given and analyzed.

The first case was that of a female, twenty-two years old, who was treated since the age of twelve for rheumatic heart disease and, in the last years, for pleural effusion, icterus, ascites and enlargement of the spleen as a result of right cardiac insufficiency. Roentgen examination revealed increased markings extending into the periphery with coarse meshwork and isolated small nodules in the middle and lower lung fields. The heart was moderately enlarged to the left and measured 14 cm. at the base. The pulmonary arc was superimposed on the entire left hilus and was unusually prominent. The diameter of the branch of the pulmonary artery for the right lower lobe measured 20 mm. There were strong pulsations in the region of the pulmonary arc and both hili. After two weeks her condition deteriorated greatly with increase of the cyanosis and a feeling of oppression, fever up to 102.2° F., leukocytosis of 17,000 with neutrophilia and moderate eosinophilia, ascites, edema of the legs and a sedimentation rate of 54 mm./1 hr.(W). A chest roentgenogram before death showed, in both middle and lower lung fields, nodules up to rice grain size, confluent in places, forming a meshwork of markings. The heart was enlarged to the left with a basal diameter of 14.5 cm. There was prominence of the pulmonary arc with increased pulsation. The right lower lobe artery measured 27 mm. Autopsy showed arteritis of the small pulmonary arteries with perivascular edema, atherosclerosis of the large pulmonary branches, emphysema, bronchitis, marked hypertrophy and moderate dilatation of the right ventricle, subepicardial hemorrhages, congestive swelling of the spleen and congestive cirrhosis of the liver with thickening of the capsule. In addition to the older fibrotic changes of the vessels, an acute inflammatory phase of a pulmonary arteritis could be followed roentgenologically in this case, corresponding to findings described in primary pulmonary arteritis as well as in acute periarteritis nodosa.

The second patient, a fifty-six year old man, was treated for emphysema, bronchitis and insufficiency of the right heart. In this patient the disseminated arteritic foci were less clearly visible roentgenologically and appeared as increased bands, coarse meshwork and as a partially fleck-like design. The emphysema and bronchitis overshadowed the vascular changes.

The simultaneous occurrence of pneumonic infiltrations and periarteritis was demonstrated in the third case which was that of a forty-two year old woman.

After a discussion of the literature the author concludes that pulmonary arteritis is the most frequent cause of "primary pulmonary sclerosis" and is characterized roentgenologically by four different stages. (1) The acute stage shows small unevenly distributed flecks in coarse meshwork sparing the apices; they represent the vascular changes. In case of paravascular infiltrations and edema, soft blotches extend from the hilus and may be resorbed quickly. (2) The subacute stage is roentgenologically less conspicuous and shows a coarse meshwork and fine nodules (larger flecks may indicate small aneurysms). Complications, such as infarcts, pneumonic infiltrates and small pleural effusions, are sometimes seen in the acute and subacute stage. In case of minor vascular changes the right heart and main pulmonary branches remain uninvolved, while lasting difficulties in the lung circulation lead to dynamic as well as organic disturbances. The disparity between minor clinical and extensive roentgenological findings is often striking. Death may occur from cardiac decompensation, ruptured aneurysm, arteritis of heart, kidneys, brain or other sequelae. (3) The latent stage is dominated by increasing cardiac adaptation; pulmonary symptoms are atypical and insignificant. (4) The last stage is a result of the extensive obstruction in the lung circulation with a fully developed cor pulmonale. The lungs may show denser markings and sometimes the emphysema may dominate the picture. The main stem of the pulmonary artery is considerably dilated and pulsates vigorously. The maximum duration of the described sequence is twenty years, more often much shorter.—*Hans F. Plaut, M.D.*

Bass, Hyman E., Greenberg, David, Singer, Emanuel, and Miller, Milton A. Pulmonary changes in uremia. *J.A.M.A.*, March 1, 1952, *148*, 724–726.

The pulmonary changes in uremia have been described as increased densities, confined predominantly to the hilar zones in a bilateral symmetrical fashion, with clear basal and peripheral zones. It was soon recognized that these changes were not limited to uremic patients, but might occur in certain types of pneumonia.

The authors observed a group of 8 patients with pulmonary changes associated with uremia. All 8 died. The heart shadow was usually enlarged and death in some cases appeared due to anoxia.

Grossly the uremic lungs showed a consolidation of the inner aspect with the outer lung zones normally aerated. Hyaline membranes and hyaline deposits in the alveoli were common features. The resemblance to rheumatic pneumonia is marked.

The pulmonary changes as described are most likely to occur in uremia due to glomerulonephritis. They indicate a poor prognosis, are usually associated with dyspnea and occasionally hemoptysis. Altered pulmonary capillary permeability is probably the fundamental cause.—*Arthur B. Smith, M.D.*

SUTER, F., and ISELIN, H. Hat die tuberkulöse Hiluslymphknotenperforation beim Erwachsenen praktische Bedeutung? (Does perforation of tuberculous hilar lymph nodes in adults have practical significance?) *Schweiz. med. Wchnschr.*, March 15, 1952, *82*, 273–282.

In children, perforation of hilar lymph nodes into the bronchial lumen is considered a serious form of the disease because it often represents the beginning of tertiary tuberculosis of the lungs. However, in adults, such a condition is not so considered because the anatomical relationship of the bronchial tree is different than in a child and also because primary tuberculosis in adults is relatively infrequent. The authors attempt to show that the tertiary form of tuberculosis of the lungs as a result of perforation of the hilar lymph nodes may also occur in adults.

Up to the present, the following opinions regarding the origin of tuberculosis of the lungs existed: The primary focus may enlarge, become necrotic, and lead to new foci. By hematogenous routes, or more likely by means of the hilar lymph nodes, the disease may spread from the primary focus to other areas, usually in the apices of the lungs, from which later the tertiary form originates. After the primary complex has disappeared, an exogenous reinfection may occur with the formation of a new focus from which the process may progress.

Recently, Schwartz and also Uehlinger have shown on the basis of pathological-anatomical studies, that the bronchial spread as a result of perforation of hilar lymph nodes occurs more frequently than it has been believed previously. Also, in resections of the lung for tuberculosis, one almost always sees a large partially caseating pack of lymph nodes in the region of the hilus, which nodes are associated intimately with the bronchial tree. Roentgenologically, these nodes may not be seen. In contrast to children where perforation of hilar lymph nodes is not a seldom occurrence, that in adults, according to the literature, appears to be much more rare. The authors believe that the reason for this is that in adults the lumen of the bronchial tree is much wider than in children and that the elasticity of the bronchi has decreased. As a result, more frequently the segmental bronchi become involved. The perforation need not be large, but may produce only a fistula. Not all preforations of hilar lymph nodes need be followed by massive lung findings, but more frequently may be manifested by minor changes in the lungs.

With involvement of the hilar lymph nodes, the adjacent lung tissue becomes affected and since the bronchial tree is in direct relationship with the lymphatics, it is involved relatively frequently. For the lungs to become involved, there must first be a narrowing of the lumen of the bronchus by compression from without or through edema, inflammation, and granuloma formation of the mucosa. This leads to atelectasis. Secondly, caseating purulent tuberculous material must be present in appreciable amounts. This material would usually come from perforated lymph nodes. It is highly questionable whether small "soft" lung foci produce massive bronchogenic spread as frequently as pathologists and clinicians believe at present. As long as the bronchial system remains intact, this possibility is extremely unlikely. In the presence of large cavities with abundant secretions, such a relationship no longer exists.

Involved hilar lymph nodes bring about the following manifestations on the bronchi: (1) compression of the bronchus (particularly in children); (2) lymphogenous spread of the tuberculous process into the mucosa, with the formation of localized infiltrations, tuberculomas and ulcers; (3) frequent perforations into the lumen of the bronchus.

Many case histories are presented demonstrating extension of tuberculosis into the lungs, secondary to lymph node involvement. The authors discuss the problem of the frequency of perforation of lymph nodes into bronchi. In the past eleven months, 537 adults were bronchoscoped because of tuberculosis in the lungs and 21 were found to have definite bronchial perforations. Not all perforations lead to complications in the lungs. Residual infection in the bronchus need not produce clinical symptoms since a spread may have healed, or the lung finding was so interpreted that bronchoscopy was not considered necessary. Limitations in bronchoscopy may cause a missing of some perforations.

In general, the authors found approximately 10 per cent of the bronchoscoped patients to have perforations and residual infiltrations in the bronchi. The resulting symptoms were usually minimal. The one single suspicion in the great majority of perfo-

rations was the presence of changes in the lungs described in the case reports.

The localization in the bronchial tree showed nothing remarkable except for the fact that in the upper lobe bronchi the right side was always involved from below, and on the left from above. The location of the residual infiltration favored the lower lobe predominantly on the right side. Roentgen examination even with laminagraphy suggested perforation in only 10 cases. In the others, the findings were either negative or interpreted incorrectly otherwise. No abnormality was found in 6 cases where roentgen examination reported the larger bronchi to be involved.

Three typical cases demonstrating the course of a perforation into the bronchi are presented. Three stages of the course are noted: (1) perforation with more or less granulation around an ulcer, with caseating or purulent material and spread into the distal parts of the lung; (2) granulation with some tumor masses, without definite demonstration of a fistula; (3) scarring, in which the whole process disappears spontaneously for the most part and the residuum is outlined quite discretely.

The authors believe that conservative local treatment is indicated, particularly with the use of streptomycin, PAS, etc. Collapse therapy is absolutely contraindicated, since a disturbance of drainage as well as of aeration will be aggravated with all the well known catastrophic complications in the lungs.

Bronchogenic spread, in the absence of considerable secretions, may occur only if there exists severe disturbance of aeration, of the cough reflex, and of the epithelial cilia, or if stenosis causes retention of secretions. Circumscribed mucous membrane infiltrations or even ulcerations, which may result in scars similar to those of a perforation, seldom cause such spread. Given a bronchogenic spread, with drainage conditions normal and in the absence of bleeding or large lung infiltrations, the suspicion of perforation into a bronchus from a lymph node is to be considered seriously and immediate confirmatory bronchoscopy should be done.

In conclusion, perforation into the bronchi by hilar lymph nodes is not a rare occurrence in adults. This may lead to pneumonic infiltrations or bronchogenic scattered deposits, which may be found isolated in one entire lobe or in individual segments. Clinical and roentgen findings of hilar lymph node perforations frequently are so slight that only bronchoscopy may clarify the diagnosis. This is done on the basis of residua in the bronchus secondary to previous perforation. Treatment is predominantly local with aspiration of the perforation area, combined with positioning of patient to improve drainage of the involved portion of the lung. Streptomycin and PAS appear to be of aid. Collapse therapy is contraindicated in the presence of a fistula because drainage is made worse.—*Samuel Richman, M.D.*

Veeneklaas, G. M. H. Cause and sequelae of intrapulmonary shadows in primary tuberculosis. *A. M. A. Am. J. Dis. Child.*, March, 1952, *83*, 271–281.

The author states that primary type pulmonary tuberculosis is considered to be principally a disease of the lungs. The great importance of the bronchi has received little attention. Their role is probably most clearly demonstrated by cases in which lobar or segmental shadows are present. This paper is a review of the current knowledge concerning these shadows.

Pathological, bronchographic and bronchoscopic investigations in recent years have revealed that the shadows are caused by bronchial obstruction, either because a tuberculous lymph node involves the bronchial wall in the disease process or because it perforates into the bronchial lumen. Tuberculosis of the bronchial wall causes edema, hyperemia, submucous tuberculomas, ulceration, perforation resulting in small fistulas (one or more) or in a large opening and after perforation, formation of granulation tissue. With sufficient narrowing of the bronchus, natural drainage becomes impaired. Secondary inflammation will easily arise behind the obstruction (obstructive pneumonitis, obstructive pneumonia). The perforated lymph node may contain tubercle bacilli. When these are aspirated, they may cause tuberculous foci in the area beyond the obstruction. Moreover, the primary focus may be situated in the dense, shadowed area. Bronchiectases as a residue of the primary shadows have been described.

The marked residual lesions of the bronchi found after primary pulmonary tuberculosis are usually symptomless and occur without or with only slight changes in the roentgenogram of the chest. The author found that in 30 of 51 patients with lobar or segmental shadows, these were noted one to sixteen years after the discovery of the original shadow. His principal findings were stenosis, ectasia, severe shrinking, and marked growth. With one exception these lesions were found in the upper lobes, the middle lobe and the lingula, and they did not give rise to symptoms. The one exception, the patient with stenosis and ectasia of the lower lobe, had symptoms. The residual shadows in the right middle lobe and the left upper lobe are probably often to a large extent due to pleural thickening, in the author's opinion.

The lesions are described in detail in the paper and illustrated by 10 roentgenograms.—*Ralph S. Bromer, M.D.*

Lichtenstein, M. R., and Bettag, Otto L. Criteria for sanatorium care of children with tuberculosis. *A. M. A. Am. J. Dis. Child.*, March, 1952, *83*, 292–300.

The authors' intent in this paper is to clarify the criteria for admission to sanatoria of children with

tuberculosis and to discuss some of the issues involved. Under the heading of diagnosis, the following types of tuberculous involvement are discussed: Type I, primary tuberculosis with positive tuberculin reaction and normal roentgenogram; Type IIA, primary infection with large hilus nodes shown on the roentgenogram; Type IIB, primary infection with massive nodes causing atelectasis; Type IIC, primary infection with large parenchymal component; Type III, progressive primary tuberculosis; Type IV, reinfection tuberculosis.

Sanatorium care should imply that the patient requires treatment which cannot be given at home. This includes antimicrobial therapy, collapse therapy, and surgery with all the necessary adjuvant procedures. All will agree that children with evidence of dissemination or with evidence of destructive pulmonary disease, of either the progressive primary or the reinfection type, deserve sanatorium care. Children with primary infection with massive lymph nodes causing atelectasis also deserve sanatorium care and treatment since antimicrobial therapy is indicated and bronchoscopic aspiration may be helpful.

Children with primary tuberculosis, Types I and II, who have demonstrable tubercle bacilli in the gastric contents, are considered by the authors to be most likely noncontagious and therefore should not be placed in a sanatorium nor be kept home from school. The authors contend that a considerable number of children are unnecessarily placed in sanatoria, resulting in possible exposure, excessive therapy, and waste of valuable bed space.

The question of streptomycin therapy in primary tuberculosis is also discussed. Five roentgenograms are reproduced showing the four diagnostic types of the disease.—*Ralph S. Bromer, M.D.*

PACHECO, CARLOS R., and DEL CASTILLO, HERMILO. Angiographic studies after pulmonary resection. *J. Thoracic Surg.*, March, 1952, *23*, 262–271.

Thirteen cases of pulmonary resection (either lobectomy or pneumonectomy) were studied angiographically. In these cases no method was used to fill the cavity remaining after pneumonectomy or lobectomy.

The mediastinum was found to be displaced toward the operated side. This displacement was more marked as the time between pneumonectomy and angiography increased. In lobectomized patients the angiograms demonstrated a diminished blood supply to the other lobes. In all cases there was an overdistention of the other lung after pneumonectomy or of the other lobes after lobectomy.

The authors believe that allowing the rest of the lobes or the other lung to re-expand and fill in the cavity left after lobectomy or pneumonectomy gives rise to a state of respiratory insufficiency. The substitution of the lung tissue extirpated by a collapse method may be useful to prevent the total re-expansion of the rest of the pulmonary tissue. They condemn pneumonectomy from a functional point of view, and advocate the extirpation of as little pulmonary tissue as the disease may allow in order to prevent respiratory insufficiency.—*Thomas C. Stansbury, M.D.*

STOREY, CLIFFORD F. Encapsulated pleural effusion simulating mediastinal tumor; report of two cases. *Radiology*, March, 1952, *58*, 408–414.

Two cases of encapsulated paramediastinal pleural effusion simulating mediastinal tumor are reported. Spontaneous regression of the lesion to total disappearance occurred in both patients. Both showed mild peripheral pleural effusion at some time during the course of the disease. The first case was of undetermined etiology, associated with cough and fever, while the second was tuberculous in origin. The latter patient, at thoracotomy, was found to have broad bands of adhesions at the site of the former effusion. The smooth, rounded shadow cast by the encapsulated fluid was far anterior and overlying the left heart border in both patients.—*William A. Goodrich, Jr., M.D.*

HOHN, MATHIAS. Über den Wert der Bronchographie für die Diagnose bei Tumoren des Mediastinums. (The value of bronchography for the diagnosis of tumors of the mediastinum.) *Röntgen-Blätter*, March, 1952, *5*, 79–86.

Among the many special roentgen methods of investigation of mediastinal masses, bronchography has received little consideration. In the last two and one-half years, however, the author has studied 40 cases with clinically and roentgenologically diagnosed mediastinal tumors. In all cases a bronchogram gave important information for the definitive diagnosis and surgical intervention.

By fluoroscopy and film studies the size, extent, and position of the mediastinal tumor can usually be well enough determined; bronchography shows relationship of the mass to the bronchial tree and unequivocally demonstrates in most instances the presence or absence of direct or indirect tracheobronchial involvement. Tumors involving the tracheobronchial tree are usually divided into two general groups: (1) expansile space occupying lesions, and (2) destructive space occupying lesions. Either type may be intra- or extrabronchial.

Almost all extrabronchial (expanding and eroding) space occupying lesions in the mediastinum affect the bronchial system. Expansile tumors may cause indentation, and/or displacement, and/or narrowing of the trachea or bronchial tree. The affected wall is smooth. From the displacement of the trachea

or bronchi, the direction of growth of the tumor can be surmised. An expansile extrabronchial tumor can also surround the bronchus and compress it—exhibited on the bronchogram as a simple diminution of bronchial caliber to complete closure of the bronchus.

A spreading of the main bronchi and a rounding off of the bifurcation angle speak for an expansile process in the bifurcation region.

All malignant tumors of the mediastinum (malignant primary tumors and secondary metastatic nodes) belong to the extrabronchial destructively growing processes. With these tumors the changes of the bronchial wall itself are in foreground as compared to the indentation and displacement as seen with the expansile tumors. The wall may be smooth, but often shows irregular "sawtooth" defects. Partial or complete stenosis of a bronchus or of a trachea is common. Many differential characteristic features of complete bronchial stenosis have been proposed, but the author believes that none are valid. Tumors growing extrabronchially and those growing from within the lumen both present a smooth bordered stenotic area, and they cannot be differentiated in the bronchogram on the basis of the appearance of the bronchial stump.

Several interesting illustrations are presented.—*Harold E. Fulton, M.D.*

Vögtlin, J., and Minder, W. Ueber Thorotrastschäden nach Bronchographie, retrograder Pyelographie, Salpingographie und Arteriographie. (Thorotrast injuries following bronchography, retrograde pyelography, salpingography and arteriography.) *Radiol. clin.*, March, 1952, *21*, 96–115.

As a result of an extensive review of the literature, the authors were able to compile a long list of injuries due to thorotrast administered in various ways for diagnostic purposes. This list is as follows:

After intravenous injection: aplastic anemia, panmyelophthisis, dystrophy of the liver, cirrhosis of the liver, reticulum cell sarcoma of the liver, necroses and thorotrast granulomas, especially in the organs of the reticuloendothelial system which, as is known, stores the thorotrast.

After arteriography: necrosis of the arterioles, deposition of thorotrast in the vascular walls and perivascular tissues.

After cerebral arteriography: hemiplegia, retinal and corneal changes, severe alterations of the brain substance and death.

After perivascular injection: degenerative vascular changes and thorotrast granulomas. Such granulomas were also observed after mammography, injection of fistulas and instillation of the nasal accessory sinuses with thorotrast.

After retrograde pyelography: thorotrast deposits in the kidney pelvis, focal nephrosclerosis and spindle cell sarcoma.

Thorotrast has been used only in rare occasions for bronchography, myelography and salpingography; therefore, injuries in conjunction with such applications are seldom reported.

The authors themselves during 1950 observed 4 cases of injuries due to the diagnostic use of thorotrast. These 4 cases are described in detail and amply illustrated.

In the first case, in which the thorotrast was used for bronchography, eighteen years later there was evidence of bilateral granulomas associated with primary squamous cell carcinoma of the lung. In view of the proved radioactivity of the granulomas, it is believed that the carcinoma may be considered as thorotrast-induced.

In the second case thorotrast was employed for retrograde pyelography and three years later massive thorotrast deposits were found in the renal capsule and perirenal tissues.

The third case is an example of damage following thorotrast salpingography. Roentgenographic examination three years later revealed thorotrast granulomas in the serosa of the small pelvis, in the region of the appendix and in both tubes. The question of possible radiation injury to the ovaries is raised in conjunction with these findings.

The fourth case is the most unusual of all. Cerebral arteriography was performed with thorotrast and five years later the radioactive substance was demonstrated in the liver, spleen and one mediastinal lymph node. This case furnishes indisputable proof that the thorotrast is carried by the blood stream and stored in the reticuloendothelial system.

A rich bibliography is appended.—*T. Leucutia, M.D.*

Scarinci, C., Galletto, F., and Gianturco, E. Spirometria e angiopneumografia. (Spirometry and angiopneumography.) *Arch. tisiol.*, 1952, *7*, 132–152.

The authors have attempted an evaluation of the functional capacity of the lungs of patients suffering from various pleuropulmonary conditions. They report on the study of 8 patients affected by tuberculosis, bronchogenic carcinoma, phrenic exeresis, pneumothorax, thoracoplasty, silicosis and fibrothorax. These patients were subjected to angiocardiography for the study of their pulmonary vascular bed. In addition, measurements were made of the vital capacity, air exchange per minute and oxygen consumption per minute. These measurements were done separately on each lung after obstructing the opposite main bronchus with a rubber balloon. The measurements obtained were compared with the normal standards published by Bjorkman.

In general, the results of the measurements of vital capacity, air exchange and oxygen consumption agree very closely with the information provided

by angiocardiography in its pulmonary phase. The authors, however, point out that angiocardiography is easier to perform and that it gives more detailed information regarding the lung segments affected. This information cannot be obtained by spirometric measurements, which of necessity apply to one whole lung.—*Cesare Gianturco, M.D.*

OCHSNER, ALTON, DECAMP, PAUL T., DEBAKEY, M. E., and RAY, C. J. Bronchogenic carcinoma; its frequency, diagnosis, and early treatment. *J.A.M.A.*, March 1, 1952, *148*, 691–697.

In 1912 Adler was able to collect 374 cases of bronchogenic carcinoma. Between 1938 and 1948 there was an increase of 144 per cent in the incidence of this lesion. During this same period there was an increase of 31 per cent in deaths due to all forms of cancer. In England deaths from cancer of the lung between 1922 and 1947 increased fifteen fold.

The contribution of smoking to the increase in number of cases of carcinoma of the lung is again cited and documentary evidence is presented.

The authors observed 948 cases of bronchogenic carcinoma. The average duration of symptoms prior to establishment of diagnosis and institution of treatment was 12.3 months. The incidence of resectability was only 35 per cent.

Bronchogenic carcinoma is a disease primarily affecting males and is observed more frequently in whites than negroes. Its greatest incidence is in the fifth, sixth and seventh decades with 40 per cent of the cases occurring between the fourth and sixth decades. In more than 50 per cent the primary site is in the upper lobes, there being no predilection for the right or left side. Contrary to the authors' initial impression, the main stem bronchi are rarely involved. There were only 13 cases of this type. In 188 cases the carcinoma originated in a lobe bronchus and in 123 cases it occurred peripherally.

Clinically, the disease has an insidious onset. In a man of forty-five or older, any persistent cough, peculiar sensation within the chest, or hemoptysis should be looked upon with the gravest of suspicion until carcinoma can be ruled out. Cough was present in 90 per cent of the patients undergoing resection. Weight loss, chest pain, hemoptysis, persistence of a "cold," dyspnea, and thoracic discomfort were the commonest complaints in the order mentioned.

Systematic roentgen examination is strongly urged since the incidence of resectability is much higher when the lesions are discovered early. Any shadow not readily explainable should be explored.

In the authors' series of cases undergoing resection the diagnosis of bronchogenic carcinoma was confirmed in 84 per cent.

Bronchoscopy should be done in all cases as frequently one is able to obtain a biopsy, bronchial washings, or cells for staining with the Papanicolaou technique. In addition, bronchoscopy often reveals evidence of fixation, pressure or invasion, all of which are important signs for prognostic evaluation.

The value of the cytological examination is stressed. In 112 cases so studied carcinoma was indicated in 76 per cent.

The authors feel that pneumonectomy with en bloc removal of the mediastinal lymph nodes constitutes the treatment of choice.

Of the 948 cases, 385 (41 per cent) were inoperable and 536 (59 per cent) were operable. Of this latter group 512 (54 per cent) were explored; 332 (65 per cent) were resectable, and 180 (35 per cent) were not resectable. Twenty per cent of the operated cases died in the hospital. Of special interest is the fact that of the 332 cases considered suitable for resection only 90 cases were subjected to curative surgery while 232 cases received palliative surgery.

Of the 232 patients who had palliative resection 42 per cent were living at six months, 24 per cent at one year and 10 per cent at five years. Of the 90 patients with curative surgery, 69 per cent were living at six months, 54 per cent at one year, and 38 per cent at five years.

The over-all five year survival in the 948 patients was 6 per cent. This figure seems very low; however, it must be remembered that only about 33 per cent of the entire group was resectable.—*Frederick W. O'Brien, Jr., M.D.*

SCARINCI, C. L'exploration angiopneumographique en pneumologie. (Angiographic studies of pulmonary conditions.) *Presse méd.*, March 26, 1952, *60*, 439–440.

The author has studied the vascular bed of the lungs of 5 patients with tuberculosis, 2 with bronchogenic carcinoma, 2 with silicosis, 1 with asthma, 1 with a mediastinal tumor and 1 with a lung abscess.

The excellent roentgenograms accompanying this article show the decrease of the vascularization of lungs compressed by space-occupying lesions, by pneumothorax or by thoracoplasty; the vasoconstriction which accompanies asthma; the peculiar vascular changes caused by silicosis and the compensatory increase of the circulatory bed in the uneffected lungs.

Of interest is the fact that while bronchogenic carcinoma effects the appearance of the pulmonary vessels by indenting them or decreasing their size, inflammatory conditions do not. This enabled the author to differentiate between lung abscess and carcinoma in one of his patients.

The subject of the pulmonary circulation as affected by various disease is of great interest and may become very important in establishing a diagnosis and in evaluating the possibilities of treatment—*Cesare Gianturco, M.D.*

Lackey, Robert W. Pulmonary adenomatosis (alveolar-cell tumors); report of two cases. *Radiology*, Feb., 1952, *58*, 215–220.

Pulmonary adenomatosis is a rare disease. The onset is usually insidious with gradual development of dyspnea and cough which later becomes productive. It is felt that the condition should be considered malignant since it is invariably fatal and since 50 per cent of the cases show distant metastases.

The roentgen picture may present either a nodular or diffuse type of infiltration, but fundamentally it is always nodular. The nodules may coalesce to form diffuse areas or may be marked by atelectasis or pneumonitis. In these instances, nodulation will nearly always be evident at the periphery of the diffuse process.

The differential diagnosis from various chronic granulomatous conditions is discussed.

Two typical case histories and four reproductions of characteristic chest roentgenograms are included. —*Everett E. Seedorf, M.D.*

Rubin, Morris and Berkman, James. Chondromatous hamartoma of the lung. *J. Thoracic Surg.*, April, 1952, *23*, 393–408.

The vast majority of hamartomas of the lung have been found accidentally at autopsy. In recent years, with the wide use of routine chest roentgenograms and the attitude that asymptomatic solitary lesions of the lung, which otherwise defy diagnosis, warrant exploratory thoracotomy, increasing numbers are being removed surgically.

The authors report 3 cartilaginous hamartomas of the lung removed surgically and 28 found at postmortem examination. This lesion must be considered in the differential diagnosis of all solitary rounded pulmonary lesions. A correct diagnosis may occasionally be made from the roentgen appearance of the lesion, but a definite diagnosis can be made only by exploratory thoracotomy and examination of the mass.

Because of their unique microscopic appearance and their usually superficial location in the lung, most cartilaginous hamartomas can be readily identified in the operating room and removed by simple enucleation. Lack of familiarity with the characteristics of this lesion may result in needless sacrifice of lung tissue at operation.—*Thomas C. Stansbury, M.D.*

Swan, Henry, Forsee, James H., and Goyette, Edwin M. Foreign bodies in the heart; indications for and technic of removal with temporary interruption of cardiac blood flow. *Ann. Surg.*, March, 1952, *135*, 314–323.

Foreign bodies in the heart should be removed in patients who have sepsis, emboli or pericarditis; if the foreign body lies free in a chamber of the heart; if it impinges on a valve leaflet, or myocradium during cardiac activity; and if patients have an intractable neurosis related to the presence of the foreign body. It is not necessary to remove the foreign body if it lies entirely within the myocardium.

Angiocardiography is admirably suited to identifying the anatomical location of radiopaque foreign bodies to determine whether the foreign body is embedded in the myocardium or lies within the cardiac chambers.—*Joseph Levitin, M.D.*

Stender, H. St. Ein Beitrag zum Krankheitsbild des Cor pulmonale chronicum. (A contribution to the clinical aspects of the chronic cor pulmonale.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1952, *76*, 324–331.

The circulation in the lungs and the filling of the blood vessels are indicators for the potentialities and the status of cardiac efficiency. In cor pulmonale certain changes in the configuration of the heart may give valuable information as to the condition of the pulmonary vessels and the increased pressure of the lesser circulation. The causes of the changes in the pulmonary circulation are given.

The case of a forty-four year old man is described. He complained of sudden severe stabbing pain in the left chest with respiration. There was no hematemesis. A sequence of chest roentgenograms is presented with appearance and disappearance of shadow flecks about ½ to 2 inches in diameter, somewhat increased hilar markings bilaterally and small amounts of fluid in the left costophrenic and the right cardiophrenic areas. The heart was rather vertical in position with a flat pulmonary arc and a basal diameter of 10.5 cm. which in three months increased to 12.5 cm. The right lower lobe pulmonary artery measured 14 mm. and later 18 mm. At examination, three months after admission, the right bronchial markings were considerably accentuated and the hilar vessels widened. The pulsation of the pulmonary arc was increased. On the last roentgenogram taken, about ten months after the first one and five days before death, the rounded shadow fleck in the right middle lung field had disappeared and the right lung markings were not prominent. The heart remained unchanged except for further prominence of the pulmonary arc.

Autopsy revealed massive bilateral pulmonary embolism, multiple old partially organized and several recent hemorrhagic infarctions of both lungs, and chronic emphysema. There was hypertrophy and dilatation of the right ventricle with minor interstitial myocarditis, edema of the heart muscle and thrombosis of the femoral vein.

It was thought that sedative therapy, which the patient received, was partially responsible for the lack of symptoms during most of the embolic attacks.

The development of the cor pulmonale is discussed with a review of the literature. The basal diameter

is measured from the right cardiophrenic angle to the intersection of the pulmonary artery with the left auricular appendix or the upper border of the pulmonary conus, which moves to the left as a result of the rotation of the heart. The author observed increase of the basal diameter up to 17 cm. Measurements of the diameter of the right descending branch of the pulmonary artery are often possible only in slight left rotation or on laminagrams. A formula for calculation is given. In 120 patients without suspected pulmonary vascular changes the diameter ranged from 10 to 15 mm. at 5 ft. distance. Advancing age and heavy manual labor intended to favor the higher values. In pulmonary sclerosis it was found as high as 32 mm., probably as a result of aneurysmal dilatation. The author prefers this measurement over that of the hilus after Assmann. Kymograms may show a hilar "dance" with an amplitude as great as that of the aorta. The author analyzes details of kymographic findings and their importance in the cor pulmonale as well as other cardiac conditions.—*Hans F. Plaut, M.D.*

KEIZER, D. P. R. Cor triloculare biatriatum with transposition of large vessels. *A. M. A. Am. J. Dis. Child.*, March, 1952, *83*, 333–335.

The case of a three week old boy is reported who suffered from congenital defects consisting of transposition of the great vessels, patent ductus arteriosus, patent foramen ovale, and lack of interventricular septum. Cyanosis occurred two weeks after birth. Clubbing of the fingers did not occur in the short time before death.

On the anteroposterior roentgenogram, in contrast to the lateral roentgenogram, a very narrow vessel trunk was shown with an enormously enlarged heart, overfilling of the interstices, and low lung borders because of emphysema. A clinical diagnosis was made before death of transposition of the large vessels with patent ductus arteriosus and ventricular septal defect.—*Ralph S. Bromer, M.D.*

JACOBSON, HAROLD G., POPPEL, MAXWELL H., HANENSON, IRWIN B, and DEWING, STEPHEN B. Left atrial enlargement; the optimum roentgen method for its demonstration. *Am. Heart J.*, March, 1952, *43*, 423–436.

In the diagnosis of rheumatic mitral disease (stenosis) the roentgenographic demonstration of left atrial enlargement is second only in importance to the apical diastolic murmur. The right anterior oblique view with the esophagus outlined by barium has become commonly accepted as the best single technique for demonstrating the left atrial enlargement. A critical comparative study has convinced the authors that the left lateral teleroentgenogram with barium in the esophagus is superior to the other views commonly employed. In their experience enlargement of the left atrium is generally better demonstrated in the left lateral view than in the right anterior oblique. In addition the former is more accurate in the recognition of minimal left atrial enlargement and is of value in distinguishing left atrial from left ventricular enlargement. This is due to the fact that the primary enlargement of left atrium is posterior and therefore, on spatial considerations alone, is best seen in the lateral view. The left lateral projection is preferred to the right only because the structures being studied are located slightly to the left of the midline.

Fifty men, all but one having a clinical diagnosis of rheumatic heart disease with mitral involvement, were selected for study. Uniform roentgenographic technique was used and left atrial enlargement was demonstrated in at least one view, and other evidences of left atrial enlargement (*e.g.*, elevation of the left main bronchus and double heart contour to the right of the spine) were noted when present. The degree to which both the right anterior oblique and left lateral views demonstrated enlargement of the left atrium was compared. Of the 50 cases, the left lateral view was superior to the right anterior oblique in 39. In 6 of these the enlargement could not be seen at all in the right anterior oblique but it was definite in the lateral. On the other hand, there was no instance in which the oblique view demonstrated left atrial enlargement not seen in the left lateral view.

Thus, in demonstration of left atrial enlargement, the left lateral upright film with barium-filled esophagus proves superior to the right anterior oblique in 78 per cent of 50 cases, equal to it in 16 per cent, and inferior in only 6 per cent.

The indentation and/or displacement of the barium-filled mid esophagus posteriorly by an enlarged left atrium is easily differentiated in the left lateral view from the still lower segment of the esophagus which is frequently indented, slightly displaced, or overlapped, by posterior enlargement of the left ventricle.

The technical simplicity of the left lateral view is stressed. For optimum demonstration of the left atrial enlargement in the right anterior oblique position, the patient must be positioned fluoroscopically; fluoroscopic positioning is, of course, not necessary for the left lateral film.—*Harold E. Fulton, M.D.*

SCHAEDE, A., and THURN, P. Zur röntgenologischen Diagnose der angeborenen Herzfehler mit vorspringendem Pulmonalisbogen. (The roentgenologic diagnosis of congenital cardiac defects with prominent pulmonary arc.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, March, 1952, *76*, 306–316.

The most conspicuous roentgen sign of an open ductus arteriosus Botalli is the more or less promi-

nent pulmonary arc. In this well illustrated article from the University of Bonn the authors state that it has also been a frequent source of diagnostic errors, which may have grave consequences in view of surgical treatment. They attempt to differentiate between the following congenital defects showing a prominent pulmonary arc without cyanosis; open ductus, interatrial septal defect, Lutembacher's syndrome, pulmonary vein opening into the right heart, isolated interventricular septal defect (Roger), primary pulmonary sclerosis (Ayerza), isolated pulmonary stenosis and—with reservation—Eisenmenger's complex. Some of these may occasionally show normal configuration or only minor deviation with somewhat prominent arc and are therefore so much harder to comprehend. In this group of congenital anomalies the pulmonary arc is formed by the main stem or the main left branch of the pulmonary artery and shows characteristic arterial movements in the kymogram. If the conus participates in forming the cardiac contour, ventricular movements are seen.

In recent years the authors examined about 40 cases of open ductus and as many of interatrial defects. Their diagnosis was confirmed by catheterization with gas analysis, pressure readings, cardioangiography and in some cases of open ductus by operation. Because of the difficulties of kymography in small children 30 patients with open ductus and 25 with interatrial defects underwent this examination. The latter usually show a more prominent arch and fluoroscopically increased pulsations. Sometimes the arteries for the lobes show pulsatory increase in width, thought to be caused by great change in volume. The dilated pulmonary branches enlarge the hilus shadow, differentiated from mere congestion by absence of cloudiness. Also in interatrial defects the aorta was found narrow in 21 and normal in 4 cases with diminished pulsation of the arch, while in open ductus it was normal in 18 and widened in 10 instances with increased pulsation (2 not considered because of combination with coarctation). The most revealing differential sign is supplied by kymographic analysis of the pulsation of the pulmonary arc. An intermediary diastolic wave or spike was seen in 24 cases of open ductus (3 with Fallot) while it was only present in 3 and absent in 22 patients with interatrial defect. This spike is explained by increase in volume of the pulmonary artery as a result from influx of blood under high pressure from the aorta. The detour through the ductus accounts for the entering of this wave into the pulmonary artery while in a diastolic narrow phase. The excursion of this spike depends on the degree of the shunt and was extremely distinct in aortopulmonary fistula. The 6 cases of open ductus not showing this wave include 3 with additional anomalies (coarctation, interventricular defect and acute endocarditis) having different hemodynamics.

After discussion of helpful kymographic details for identification of the contour forming cardiac and vascular segments and of the differential diagnosis of other congenital defects, the authors enumerate the following significant points. In open ductus arteriosus direct catheterization of the ductus is seldom successful, systolic and diastolic pressure readings in the pumonary artery are high, approaching those in the aorta, the O_2 content of the blood in the pulmonary artery is higher than in the right ventricle as result of admixture of arterialized blood from the aorta, and angiocardiography form the venous side shows long lasting filling of the pulmonary artery with dye because of refilling from the ductus. In defect of interatrial septum the catheter can be advanced through the defect into the left atrium, the pressure is moderately elevated in the right ventricle and pulmonary artery, the O_2 content of the blood in the right atrium is definitely increased as compared to that in the vena cava as a result of influx of arterialized blood from the left atrium and there is long lasting filling of all chambers (global heart) because of circulation of the contrast medium in a short circuit through the defect.

In conclusion the findings in other anomalies by means of these special procedures are described.—*Hans F. Plaut, M.D.*

Slater, S. R., Kroop, I. G., and Zuckerman, S. Constrictive pericarditis caused by solitary metastatic carcinosis of the pericardium and complicated by radiation fibrosis of the mediastinum. *Am. Heart J.*, March, 1952, *43*, 401–412.

Solitary, diffuse, metastatic carcinoma of the pericardium producing solely and primarily the clinical picture of chronic constrictive pericarditis has not been previously reported.

A fifty-two year old white woman was studied by the authors because of intractable edema of 2½ months' duration, dyspnea, and cough. Fourteen years previously a left radical mastectomy had been performed for duct carcinoma, grade 2 (Broders). Roentgen therapy had been given to the left parasternal area and to the left axilla. A cough, attributed to pulmonary fibrosis of the left upper lobe, began soon after the radiation therapy and continued unabated for the fourteen years. Clinical and laboratory examinations of the patient suggested the presence of constrictive pericarditis. Fluoroscopy and kymography showed a small heart, surrounded by pleural adhesions, which exhibited poor pulsations. There was complete collapse and fibrosis of the left upper lobe.

The patient died during cardiac surgery and postmortem examination showed obliteration of the pericardial cavity and replacement of the epicardium by tumor cells of similar type to those of the original breast lesion. The myocardium was not involved. The left upper lobe parenchyma was replaced by hyalinized connective tissue.

Thus, a carcinoma of the breast, successfully resected fourteen years previously led to solitary metastasis to both layers of the pericardium. A scirrhous stromal reaction to the neoplastic cells accounted for the dense constricting pericardial tissue. The authors believe that radiation "contributed to the fibrosis but was not responsible for the constrictive pericarditis."—*Harold E. Fulton, M.D.*

Bierman, Howard R., Perkins, Evan K., and Ortega, Paul. Pericarditis in patients with leukemia. *Am. Heart J.*, March, 1952, *43*, 413–422.

The two major cases of death in leukemic patients have been infection and hemorrhage. Recent use of antibiotics and transfusions have reduced these fatal complications and other complications are becoming more prominent. In the past few years an increasing number of patients with leukemia have been observed terminally to present findings indicative of cardiac failure. Of 43 consecutive patients with leukemia observed at the Laboratory of Experimental Oncology, University of California, School of Medicine, 5 had pericarditis as an autopsy manifestation. Leukemic pericarditis causing functional impairment during life has generally been considered unusual and accorded an insignificant roll in the course of the disease. However, the authors now report 4 cases of leukemia in which pericarditis appeared as a serious complication and contributed toward death in 3 of the patients. Two patients with lymphogenous leukemia showed acute fibrinous pericarditis with effusion and infiltration of pericardium with lymphoid cells. One patient suffering from the myelogenous form showed an organizing fibrinohemorrhagic pericarditis with effusion; another had adhesive pericarditis with cardiomegaly and focal infiltration of the myocardium. The latter patients showed roentgen signs of pericarditis with effusion and cardiac failure prior to death.

The sudden appearance of cardiac symptoms in the absence of previous cardiac disease in a leukemic patient should make the clinician suspicious of leukemic infiltration of the heart or pericardium. Roentgenography may help, as it did in one of the cases presented, in demonstrating pericardial effusion.—*Harold E. Fulton, M.D.*

Abdomen

Fischer, Ludovig. Röntgenbefunde bei der "digestiven Megasplanchnie." (Roentgen findings in "megalosplanchnia of the digestive tract.") *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Feb. 1952, *76*, 205–212.

Dilatation and lengthening of portions of the gastrointestinal tract have their etiology in congenital, obstructive and functional factors. Mega-esophagus and megacolon are the best known changes. The author bases his observation on 100 patients from certain areas of Brazil where the disease appears to be more frequent. Only 3 cases revealed evidence of obstructive lesions while the remainder fell into the category of functional disorders. In 40 per cent mega-esophagus was associated with megacolon. In these cases the roentgen examination frequently revealed association of dilatation in one portion of the gastrointestinal tract with spastic changes in another. In some patients concomitant dilatation of esophagus, stomach, duodenum, colon and sigmoid was observed.

The incipient changes, *e.g.*, delay in emptying of the esophagus, increased peristalsis and antiperistalsis, slowly progress to true mega-esophagus with barium retention for days or weeks. Early intensive therapy is advocated. If cardiospasm prevents barium filling of a dilated stomach or duodenum, the Valsalva maneuver may be of help. Six patients of 63 showed a definite dilatation of the first portion of the duodenum. In cases of megacolon and megasigmoid, spastic zones frequently alternated with dilated ones. This is in keeping with Bodian's observations who found a paucity of ganglion cells in Auerbach's plexus in segments of spastic contraction.

The etiology of enteromegaly is not fully understood. The frequent involvement of more than one segment, association with megalo-ureter, cardiac arrhythmias and histopathological findings point toward a disease of the autonomous nervous system. The patients observed by Fischer were mostly from poorer classes and from geographic areas where pellagra is not infrequent. The onset of the disease in females often followed gestation. When vitamin B_1 deficiency proved to be the etiologic factor in enteromegaly an initial cardiospasm with the subsequent malnutrition only further enhanced the process.—*Kurt Benirschke, M.D.*

Persky, Lester, and Frank, Edward D. Foreign-body perforations of the gastrointestinal tract; a report of six cases. *New England J. Med.*, Feb. 7, 1952, *246*, 223–224.

The authors report 6 cases of foreign body perforation of the intestines. Three fish bones, two toothpicks, and a wood sliver were the offending agents.

In no case was the correct etiology suspected. The clinical findings usually led to a diagnosis of carcinoma or abscess. None of the foreign bodies was demonstrable by roentgen examination.—*Arthur A. Brewer, M.D.*

Williams, Mark H., and Johnson, James F. Mediastinal gastric cyst; successful excision in an eight-week-old infant. *A.M.A. Arch. Surg.*, Feb., 1952, *64*, 138–147.

The authors present a case of mediastinal gastric cyst occurring in an eight week old infant and treated successfully by surgical excision. This is accompanied

by a comprehensive review of 32 similar cases reported in the literature.

Although gastric cysts are rare in the general group of mediastinal tumors, they are relatively common in infancy and assume added importance when one considers that they usually produce distressing symptoms and will lead to fatality if left untreated. Most of the lesions extend into the right chest from their origin in the posterior mediastinum, where they are closely associated with the outer layers of the esophagus in its mid one-third. Although there may be a common muscular coat shared by the cyst and esophagus there has been no reported instance of an interluminal communication between the two.

As would be expected, the symptoms have generally been those resulting from pressure against the tracheobronchial tree, esophagus and adjacent lung secondary to the presence of an enlarging intrathoracic mass. In some cases pressure necrosis of the esophagus or peptic ulcer of the gastric mucosa with penetration into a bronchus and bleeding have occurred as complications. The roentgen appearance is described as that of a smoothly rounded mass containing no calcification and no air fluid level.

The authors feel the preoperative diagnosis of a mediastinal tumor is all that is necessary and indicate that some of the more refined diagnostic procedures such as needle aspiration may be more hazardous than helpful. The proper treatment has proved to be thoracotomy and excision of the lesion with careful dissection at its attachment to the esophagus in order to obviate the danger of damaging the esophageal blood supply.—*James Martin, M.D.*

Lahey, Frank H., and Marshall, Samuel F. The surgical treatment of peptic ulcer. *New England J. Med.*, Jan. 24, 1952, *246*, 115–123.

This article is a review of 16,000 cases of peptic ulcer in which 1,600 partial gastrectomies have been performed. Several questions in regard to the management of peptic ulcer, especially the surgical aspects, are discussed. When should surgery be resorted to in peptic ulcer? The mortality in cases of duodenal ulcer treated by partial gastrectomy is related to the degree of involvement of the head of the pancreas and common bile duct. These complications could be diminished if physicians would place a limit on the number of acute ulcer episodes their patients may undergo before coming to surgery.

The use of banthine in the treatment of peptic ulcers was tried in 100 cases. Of this group 11 were unable to tolerate the drug; 30 developed recurrence of ulcer symptoms while taking the drug. They feel that banthine is a useful addition to the medical management, but it cannot be used alone in the treatment of duodenal ulcer with no need of surgery.

When to operate on a patient with massive hemorrhage from duodenal or gastric ulcer? From the authors' experience no patient who has bled seriously is in too poor condition due to exsanguination to be operated on for control of bleeding. They feel that to wait until everyone is certain a surgical procedure should be performed is to create a mortality that is prohibitive. The most factual indication for immediate operation is when the total blood volume drops below 60 per cent.

The problem of recurring pyloric obstruction is met with operative procedures when the condition has existed for three months or more. The Wilkinson drainage test is also used in evaluating these cases.

The question of malignancy in gastric ulcer is stressed as an indication for surgery in all ulcers that do not heal promptly and remain healed.

The dumping syndrome has not been a problem in their series of 1,600 operative cases. They feel this is probably because of the Hofmeister type of anastomosis used.

Pancreatitis is a real hazard to surgery and the serious consequences are due to the fact that it frequently results in digestion of the suture material, edema, swelling and necrosis of the duodenal stump.

Vagotomy should be used in treating those cases in which an adequate partial gastrectomy has failed. It is thought the addition of vagotomy to gastric resection has not improved the results of this operation. Earlier partial gastrectomy in ulcer patients under medical management is urged.—*Fay H. Squire, M.D.*

Swynnerton, B. F., and Truelove, S. C. Carcinoma of the stomach. *Brit. M. J.*, Feb. 9, 1952, *1*, 287–292.

The experience at the Radcliffe Infirmary with carcinoma of the stomach has been reviewed for the period of 1938–1949, during which time 375 cases were followed, the length of follow-up varying from one to 13 years. Every case was adequately observed and recorded.

Age and length of history. Twice as many men as women were seen and in each sex the peak incidence occurred in the sixties. Nearly half of the patients were admitted within six months of their first symptom, while at the other extreme nearly 1 in 5 had symptoms lasting for more than two years.

Site of lesion. The distribution was as follows: pyloric end, 58.1 per cent; body, 21.4 per cent; cardiac end, 12 per cent; diffusely infiltrating, 8.5 per cent. The diffusely infiltrating type was found in 14 per cent of patients below the age of sixty as against 3.8 per cent above the age of sixty; otherwise age and sex had little influence on the site of the lesion.

Symptomatology. More than 4 out of 5 patients began their illness with symptoms referable to the gastrointestinal tract, the majority suffering from some type of "indigestion"—which was extremely variable. Dysphagia was fairly common in lesions of the cardiac end of the stomach. Hematemesis or melena, while being present in 77 of 375 cases, was not more frequent in lesions of the cardiac end.

Associated conditions. In 26 of 375 cases, there was some evidence that the neoplasm might have arisen from a simple gastric ulcer. The authors are aware of the controversy in regard to "ulcer-cancer" and believe that a minority only of these 26 cases were truly examples of such. In 4 instances a history of pernicious anemia antedated the development of carcinoma, conforming to the observations of Kaplan and Rigler that patients with pernicious anemia are unduly prone to develop carcinoma of the stomach.

Investigations. The barium meal roentgen study is the most accurate single method. The radiologists reported a gastric abnormality in 90.5 per cent at the first examination. If repeat studies are included this figure rises to 95.6 per cent. Achlorhydria is common, and is independent of the age of the patient or site of the neoplasm. However, normal or unusual acid secretions were found in 1 of every 4 patients with carcinoma and are no bar to the diagnosis of cancer. In 100 cases of proved duodenal ulcer only 2 per cent had achlorhydria, while in 100 cases of simple gastric ulcer 25 per cent had achlorhydria or hypochlorhydria. As is well known to gastroenterologists, the fractional meal has a limited diagnostic value in carcinoma. Occult blood was present in large or moderate amounts in 84 per cent. Gastroscopy was carried out in 33 patients, with the following results: right diagnosis 21, wrong diagnosis 5, unsatisfactory examination 7.

Length of history and prognosis. In the resected group of cases, the longer the history, the better the prognosis. It is believed that this finding is due to the likelihood that the neoplasm is a slow-growing one if symptoms have lasted more than two years and the growth is still suitable for resection. 23.3 per cent of the resected group were alive at five years; only 1 of the non-resected group survived five years.

In conclusion, the authors state that the "barium meal examination is the surest way of demonstrating the presence of a neoplasm and ideally it should be carried out as a routine in all patients over forty who develop indigestion." "If the barium meal study is negative and the indigestion persists, further barium meal examinations should be carried out."—*Chauncey N. Borman, M.D.*

MORGAN, RUSSELL H., and STEWART, HAL B. Clinical experience with telepaque, a new gallbladder compound. *Radiology*, Feb., 1952, *58*, 231–234.

An evaluation of the clarity of gallbladder visualization and the clinical reactions to the opaque media was made on 200 patients to whom telepaque (3 gm.) and iodoalphionic acid (priodax, 3 gm.) were administered alternately.

Telepaque produced approximately 35 per cent greater opacification of the gallbladder by densitometric study than iodoalphionic acid. Also 40 per cent fewer patients required a second dose of the opaque medium for satisfactory visualization of the gallbladder in the telepaque series than in the iodoalphionic acid group.

Clinical reactions from telepaque were found to be extremely mild and of less frequent occurrence than with iodoalphionic acid.—*Everett E. Seedorf, M.D.*

BLEGEN, H. M., SWANBERG, A. V., and COX, W. B. Entrance of common bile duct into a duodenal diverticulum; report of a case corrected by surgery. *J.A.M.A.*, Jan. 19, 1952, *148*, 196–197.

The authors point out the rarity of the entrance of the common bile duct into a duodenal diverticulum and state that they were able to find only 5 such cases reported in the literature prior to 1949. In all of these, the anomaly was found at autopsy.

They describe a case in which the roentgenograms of the upper gastrointestinal tract revealed a large lesion in the second portion of the duodenum which was thought to be a diverticulum or tumor. There was also a deformity of the duodenal cap due to ulcer. Cholecystograms showed a normally functioning gallbladder.

Exploration revealed the presence of this anomaly which is well illustrated with drawings. Also, the postoperative reconstruction is illustrated.

In view of the fact that 65 per cent of all duodenal diverticula occur in the second portion of the duodenum near the ampulla, the authors are surprised that this anomaly is not found more frequently. It is probable that, due to the silent nature of the diverticulum, many of the cases are overlooked. They stress that the existence of the lesion in all patients reported was discovered only after painstaking effort and that the symptoms were minimal. They speculate on the relationship between the ulcer and the diverticulum, stating that it seems probable that the accumulation of bile in the diverticulum may have interfered with the proper neutralization of the gastric juices in the first portion of the duodenum, thus making the mucosa in that area more susceptible to autodigestion and ulceration.—*R. D. Moreton, M.D.*

ROYER, MARCELO, ARENAS, JOSÉ V., and MAZURE, PABLO A. La colangiografía laparoscópica en el diagnóstico de los tumores de vías biliares y páncreas. (Laparoscopic cholangiography in the diagnosis of tumors of the biliary ducts and pancreas.) *Prensa méd. argent.*, Feb. 22, 1952, *39*, 334–340.

In addition to the advantage of direct inspection of the abdominal viscera for purposes of biopsy, etc., laparoscopy provides a means of obtaining cholangiographic visualization of the biliary ducts. Ten cases were examined by this method, 9 of which were jaundiced. In 5 of these cases, the diagnosis was confirmed by histological examination. These included carcinoma of the gallbladder, tumor of the papilla

of Vater, tumor of the common duct, benign tumor of the common duct and adenocarcinoma of the liver.—*Murray M. Friedman, M.D.*

Biondetti, Paolo. Strato orizzontale trasparente. (Transparent horizontal stratum.) *Ann. radiol. diag.*, 1952, *24*, 53–84.

The author reports a case of chronic cholecystitis. This patient developed attacks of vomiting, and the presence of bile and gallstones of uniform size were frequently found in the vomitus. This case was thoroughly studied both with intravenous and oral methods of cholecystography. He advocates the use of the upright and right lateral decubitus position to study this "layering" effect of non-opaque stones. The gallbladder was as well visualized with the oral as with the intravenous method. It was noticed that as the concentration of the radiopaque medium increased in the gallbladder, the layer of transparent stones would be displaced from the most dependent position of the gallbladder to a higher level. He found that soon after administration of water the opacity of the gallbladder increased, whereas intramuscular injection of decholin decreased the degree of opacity. Ingestion of egg yolks caused the entire gallbladder to be opacified and uniformly visualized.

After surgery the gallstones in this case were found to be composed of cholesterol and had a specific gravity of 1.042 to 1.049. Since normal bile in the gallbladder has a specific gravity of approximately 1.033 with variations of 1.012 to 1.050 and the iodinated bile has a specific gravity of 1.042 to 1.056, the transparent horizontal stratum becomes possible through the function of the gallbladder to concentrate the bile. The author concludes that "layering" of stones is an artefact of cholecystography.—*Peter E. Russo, M.D.*

Levine, Robert M., and Ripstein, Charles B. The diagnosis and surgical management of gall stone ileus. *Canad. M.A.J.*, Feb., 1952, *66*, 113–116.

The authors describe 4 cases of this interesting but uncommon type of obstruction of the small bowel by a gallstone. The gallstones may enter the intestinal tract either via the cystic and common duct or through an internal biliary fistula between the gallbladder and the bowel. The usual course of events is acute gangrenous cholecystitis with cholelithiasis, perforation, and subsequent fistula formation into the duodenum. Occasionally the stone may pass into the stomach or the large bowel. The size of the calculus is critical in that stones of less than 2 to 3 cm. in diameter will pass spontaneously. It is thought that mechanical obstruction may be due to volvulus about the obstruction point. Perforation is fairly common and may be due to erosion of the intestinal wall at the site of the impaction. As the small bowel progressively decreases in diameter towards the colon, the common region of impaction is the terminal ileum or ileocecal junction. A clear cut history of cholecystitis is not the usual situation. In 3 of the authors' 4 cases the diagnosis was made preoperatively by roentgen examination. The points to be noted on the film are: (1) evidence of acute or subacute small intestinal obstruction, (2) opaque gallstone within the bowel lumen, (3) air or contrast medium in the biliary passages indicative of a cholecysto-enteric fistula, and (4) a previously observed gallstone displaced into the intestinal tract. The authors quote Rigler, Bowman, and Noble in stating that in retrospect they were able to make a positive diagnosis in 13 out of 14 cases of obstruction by a gallstone from the roentgen findings alone. In the surgical management of these cases decompression is necessary preoperatively and the electrolyte balance should be restored to normal before surgery. When possible the stone should be milked proximally so that it can be removed in a healthy portion of the bowel with a transverse incision. The authors emphasize that no attempt should be made to repair the cholecysto-enteric fistula at the time of the removal of the stone.—*T. D. Allison, M.D.*

Albot, Guy, and Zérolo, Jean. Déformations de l'antre prépylorique de l'estomac dues à des causes extrinsèques. (Deformities of the prepyloric antrum due to extrinsic causes.) *Presse méd.*, March 26, 1952, *60*, 412–414.

A variety of extinsic factors may cause deformities of the gastric antrum. The authors mention enlargement of the liver of pancreas, perigastritis without or with gastric ulcer, filling defects due to enlarged gastric veins, and a polypoid defect caused by a localized adhesion. They point out that mucosal folds arranged concentrically, in parallel "waves" around a filling defect suggest extrinsic compression rather than intrinsic disease.—*Albert Oppenheimer, M.D.*

Meyer, Ralph R. Air-contrast study of the duodenal bulb; its importance in the diagnosis of duodenal ulcer. *Radiology*, March, 1952, *58*, 393–400.

Adequate fluoroscopic study of the duodenal cap was not possible in 25 per cent of 1,000 consecutive upper gastrointestinal examinations because the first part of the duodenum was directed posteriorly or was situated beneath the ribs. In an effort to improve on the accuracy of duodenal ulcer crater demonstration the author employed Hampton's technique of double contrast visualization. This consists of using the normal gas in the cardiac end of the stomach by a change in position of the patient. After administration of barium and normal fluoroscopic examination, the patient is placed on his back and the right hip elevated off the table about 45°. This maneuver places the gas in the duodenal cap and

films exposed with the patient in this position gave good double contrast roentgenograms in 70 per cent of 543 patients.

When compression of the duodenal cap is not possible this double contrast procedure is the only reliable roentgen method for detection of duodenal ulcer crater.—*Clyde A. Stevenson, M.D.*

Riesser, John F., and Vicas, Benedict. Gallstone impacted in the duodenal cap. *Radiology*, March, 1952, *58*, 401–404.

Roentgenographically discovered biliary calculi within the alimentary canal are usually found either at the duodenojejunal flexure or at the ileocecal junction. An infrequent site for impaction of a gallstone has been the duodenal cap. As far as is known to the authors, the following case is the first reported in the American literature.

The patient was first seen on November 11, 1949. A diagnosis of actue cholecystitis was made. This was controlled by antibiotics. Roentgenograms and fluoroscopy revealed a normal stomach and duodenal cap. Cholecystography with priodax showed no concentration of the medium in the gallbladder. Surgery was refused.

On May 13, 1951, the patient was again hospitalized after a week of nausea and vomiting. Four days later she passed per rectum a large cholesterol gallstone measuring 2 cm. in diameter. Roentgenographic examination the next day showed a large speckled, oval, radiolucent defect, freely movable within the duodenal cap. Barium passed by it freely into the duodenum. There was also a flow of barium through a short fistulous pathway into a small, irregular, contracted cavity in juxtaposition to the cap, presumed to be the gallbladder. A roentgen diagnosis of cholecystoduodenal fistula with calculus in the duodenal cap was made. Surgery confirmed this. A large pitted calculus with a smaller one adherent to it was found lying free in the first portion of the duodenum.

The authors point out that impaction usually occurs at areas of angulation (duodenojejunal flexure) and of constriction (ileocecal junction). They speculate as to the cause of the impaction in their reported case. The differential diagnosis of filling defects in the duodenal cap must include: benign and malignant neoplasm, pedunculated tumors of the stomach prolapsed through the pylorus, a foreign body or bezoar, aberrant pancreatic tissue, polyps and calculus.—*Dean Nichols, M.D.*

Feldman, Maurice, and Weinberg, Tobias. Aberrant pancreas; a cause of duodenal syndrome. *J.A.M.A.*, March 15, 1952, *148*, 893–898.

A study of the incidence of aberrant pancreas in the duodenum in 410 consecutive autopsies and a review of the literature of its distribution in the gastrointestinal tract are presented. The incidence in adults in the series was 12.5 per cent and in infants 15 per cent, a total of 13.7 per cent. Twenty additional cases were found in other autopsies and a total of 75 cases are analyzed.

Faulty embryological development results in this anomaly, and the development of the pancreas from duodenal buds probably accounts for its frequent aberrant location in the second portion of the duodenum. In the presented study the pancreas was found to be normal. The aberrant nodules were difficult to palpate and often were found only by opening the duodenal segment. They varied from flat to nodular elevations, were firm and well defined, and were usually in the submucosa although they were also found in the serosa. Others reported their location in the musculature. Eighty per cent were in the second portion of the duodenum. The majority were less than 1.0 cm. in diameter, but they varied from 0.1 to 2.0 cm. in diameter. Multiple nodules were discovered in 11 cases. The authors believe that duodenal diverticula and associated diseases of the pancreas are incidental and unrelated findings.

Although no complications were present in any of the 75 cases studied, inflammation, ulceration, adenoma, cyst, carcinoma, and obstruction or intussusception of the duodenum have been reported. The nudules grow slowly with age.

A review of the clinical records of 43 of the 57 adult cases showed no gastrointestinal symptoms attributable to the aberrant nodule. The authors believe that if symptoms do occur they must be due to a complication. The condition should be considered in cases of atypical duodenal ulcer symptoms, unexplained gastrointestinal bleeding, and high intestinal obstruction.

Since the nodules usually project to some extent into the duodenal lumen, the authors think that all nodules 0.5 cm. in diameter and larger should be demonstrable and they advocate double contrast study. In suspected cases, air is introduced into the stomach by tube or Seidlitz powder, the patient is placed on the left side for fifteen to thirty minutes, and then examined. A presumptive diagnosis of aberrant pancreas is made if a polyp-like filling defect is found. An ulcer-like deformity may be seen; but spot films showing compressed, distorted, flattened or effaced mucosal folds will help.

Compression spots may reveal this anomaly when barium-filled views fail. In the bulb the nodule produces a vacuolated area simulating ulcer, edema or polyp, and is stationary in repeated examinations. Hyperirritability of the second portion of the duodenum in the absence of ulceration should also suggest the possibility of an aberrant pancreatic nodule. Warning is given not to confuse an aberrant nodule with the small nodular defect on the mesial aspect of the second portion of the duodenum normally produced by the papilla of Vater.

The authors conclude that when a nodular lesion is found in the second portion of the duodenum, without symptoms, the case should be restudied at frequent intervals and surgery used as a last resort.—*Robert L. Raphael, M.D.*

Martin, Francis, and Massimiano, Antonio G. The nonvisualized gall bladder. *New England J. Med.*, March 27, 1952, *246*, 488–490.

The authors believe that confusion still exists concerning the interpretation of the nonvisualized gallbladder.

In their series 232 patients had cholecystectomies. One hundred and forty-five of these (62.5 per cent) were diagnosed showing calculi and at operation 140 had calculi (96.5 per cent of the 145). In only 3 cases was the gallbladder normal. Pathological reports of chronic cholecystitis were ignored.

Seventy-three gallbladders did not visualize (31 per cent of the total cases). Sixty of these showed calculi at operation (82 per cent). Eight had definite disease such as acute edema, strawberry gallbladder, etc. (11 per cent). Five were normal (7 per cent).

Fourteen cases were negative or indefinite by cholecystography (6 per cent). Four of these were negative at exploration. Only 1 showed stones. Of the entire series of 232 cholecystectomies, 203 cases showed stones 87.5 per cent).

The authors discuss reasons other than gallbladder disease which may cause nonvisualization. These include previous cholecystectomy, failure to take contrast medium, faulty absorption of the medium, liver disease, and obstruction of hepatic or cystic ducts.

They advise re-study of all cases of nonvisualization. This should not be done during an acute illness. The influence of drugs such as morphine, adrenalin and banthine is evaluated.

Patients on fat-free diets should probably be given some fat six hours prior to ingestion of the contrast medium to empty the gallbladder so that it can receive the medium.

With the above details in mind the authors believe that diagnostic accuracy of the nonvisualized gallbladder can approach 100 per cent.—*Lawrence A. Davis, M.D.*

Russo, P. E., and Cavanaugh, C. J. The gallbladder; comparison of roentgen and pathologic findings. *South. M. J.*, March, 1952, *45*, 232–234.

This is a discussion of 1,000 consecutive cholecystograms, demonstrating the high accuracy in diagnosis. The technique is stressed. Patients of average weight are given 3 grams of priodax, while heavier patients receive from 4.5 to 6 grams. Roentgenograms in various positions are taken, including upright or lateral decubitus. The fatty meal is omitted in patients with normal filling because of the variance in normal contraction. The literature is quoted in which 13 per cent of poor functioning gallbladders and 4 per cent of non-functioning gallbladders were normal.

In their 130 cases operated upon, the authors found only 1 case exhibiting poor function to have a normal gallbladder. This case had advanced cirrhosis of the liver.

In a group of 50 cases of non-functioning gallbladder after a single dose of dye, a double dose was given and 5 showed visualization of the gallbladder, which was found to be normal. This 10 per cent might have been due to some error in technique.

The conclusion is therefore reached that the error in the diagnosis of non-functioning gallbladder is 10 per cent on recheck.—*Robert J. Reeves, M.D.*

Rocco, Albert F., Hunt, R. R., and Savran, J. Acute pneumocholecystitis; case report and brief review of the literature. *Radiology*, Feb., 1952, *58*, 228–230.

A case of pneumocholecystitis is reported with a review of the literature. It is the impression of the authors that the pericholecystic infiltration of gas seen in their case, and the others in the literature, represents gas in the Aschoff-Rokitansky sinuses.

All reported cases had symptoms and signs typical of acute cholecystitis. In all but one of the operated cases stones were present. Roentgenograms showed the gas-filled gallbladder, often accompanied by pericholecystic infiltration of gas. It is agreed that the diagnosis of acute gaseous cholecystitis can be made only on roentgen examination.

This patient, a female aged forty-five, presented herself with symptoms typical of acute cholecystitis. On the initial roentgenograms a dilated, pear-shaped gallbladder was demonstrated, containing gas or air, with pericholecystic air infiltration. At operation, done after all of the gas had been absorbed, a subacutely inflamed gallbladder, containing stones, was removed.—*Arno W. Sommer, M.D.*

Lieber, Marshall M. The incidence of gallstones and their correlation with other diseases. *Ann. Surg.*, March, 1952, *135*, 394–405.

This is a statistical report based on 29,779 autopsies.

The incidence of gallstones increases with age, and is higher in the white than colored race, and in females than males.

There is a significant increase in gallstones in carcinoma of the gallbladder, diabetes mellitus, and acute pancreatitis, whereas in cases of tuberculosis the incidence is decreased.—*Joseph Levitin, M.D.*

GOLDEN, ROSS. Functional obstruction of efferent loop of jejunum following partial gastrectomy. *J.A.M.A.*, March 1, 1952, *148*, 721–724.

One puzzling postoperative complication of subtotal or partial gastric resection is an apparently functional obstruction of the efferent loop of jejunum. Repeated postoperative vomiting has been encountered in occasional patients for many years, but the association of this symptom with spasm of the efferent loop, demonstrable by roentgen examination, was not recognized until 1944.

In the majority of these cases, convalescence is satisfactory for eight to twelve days. Then, for no obvious reason, the patient begins to complain of epigastric fullness, particularly after eating, and nausea and vomiting. Continuous suction evacuation of the stomach gives persistent relief but prevents the patient from getting nourishment. The use of intravenous solutions suffices to maintain the protein and electrolytes at satisfactory levels until the symptoms disappear. This usually occurs between two and ten days after onset, but may take longer.

In this discussion the remaining portion of the stomach will be referred to as the stomach pouch, the portion of jejunum into which the stoma opens will be called the stoma loop. The efferent loop of jejunum passes caudad away from the stomach pouch and the efferent loop leads to the stomach pouch from loops proximal to the anastomosis.

The stomach pouch cannot produce peristaltic waves and empties largely by gravity into the stoma loop and efferent loop of jejunum. If the anastomosis is on the greater curvature side of the stomach pouch, as in the Hoffmeister type of anastomosis, the stomach empties rapidly with the patient erect and more slowly with the patient in the horizontal position.

In the Pólya type of anastomosis the efferent loop leads from the lesser curvature side of the stomach. Emptying of the stomach pouch is slow with the patient erect but more rapid with the patient lying on the right side.

In postoperative spasm of the efferent loop the barium is not held up at the anastomosis itself but at the junction of the stoma loop and the efferent loop or in the efferent loop 2 or 3 inches beyond the anastomosis. If a little barium passes through, the lumen of the efferent loop appears very narrow, with a normal or slightly irregular mucosal pattern. Examination after full recovery discloses prompt emptying with the efferent loop normal in width.

Moderate narrowing of the efferent loop of jejunum was found in 4 symtomless patients seven to ten days after partial gastrectomy. Three of them had considerable residual fluid in the stomach pouch after fasting overnight.

Functional obstruction of the efferent loop of the jejunum resulting from spasm occurs in a small percentage of cases after partial gastrectomy. Symptoms disappear spontaneously and the spasm is apparently due to a localized temporary disturbance in muscle function resulting from the necessary surgical trauma to the jejunum in making the anastomosis.—*Arthur B. Smith, M.D.*

GOLIGHER, J. C., and RILEY, T. RICHARD. Incidence and mechanism of the early dumping syndrome after gastrectomy; clinical and radiological study. *Lancet*, March 29, 1952, *1*, 630–636.

The dumping syndrome is very common after high gastrectomy, and in the authors' experience few patients in the early stages after this operation are entirely free from it; but it is usually mild and can be obviated by restricting the size of meals taken to three-quarters or a half of those taken before the operation. After six to twelve months the patients find that their capacity to cope with larger meals without discomfort gradually increases. In some 10–15 per cent of the cases, however, the dumping syndrome becomes severe and disabling, and these patients are so overcome by the epigastric discomfort and associated symptoms, such as lassitude, nausea and flatulence, cold sweating, flushing of the head and face, and even syncopal attacks, that they have to lie down for half an hour or so after meals.

There has been much discussion about the mechanism of "dumping." The authors agree with Hurst (1913) and Mix (1922) that it is due to the sudden distention of the small intestine by food which gravitates immediately from the resected stomach. Moreover, Muir (1949) and Machella (1949, 1950) in gastrectomy cases, reproduced the sensation of epigastric fullness by distending the distal or efferent loop of the jejunum by means of an inflatable balloon. In addition, in 5 of the authors' postgastrectomy cases, distention of the balloon of a Miller-Abbott tube, sited under roentgenological control in the efferent jejunal loop, reproduced the sensation of epigastric fullness experienced by those patients when affected by the dumping syndrome.

The authors present some clinical and roentgenological observations on the incidence and mechanism of dumping in 224 patients subjected to various forms of partial or total gastrectomy for gastric or duodenal ulcer or carcinoma ventriculi. This series, treated by one of the authors, was consecutive except that it omits 11 patients, who died of the operation, and 7, who could not be traced or showed early signs of recurrence of carcinoma and were therefore unsuitable for investigation.

The roentgen findings are summarized as follows: "The first striking feature is that after all forms of distal subtotal gastrectomy—in which the pyloric sphincter is sacrificed—the stomach remnant loses its power of active retention of food. Consequently food passes immediately under the influence of gravity from the stomach into the duodenum or into the upper jejunum, if they can accommodate it.

Only if the intestine is already filled to capacity as in the later stages of a meal, does food remain temporarily in the stomach. In these circumstances the weight of the meal is still borne by the intestine, but the distention of the small gastric remnant is perhaps valuable in increasing the capacity of the upper gastrointestinal tract for food, and in enabling the patient to take a larger meal than would be possible if the entire stomach had been removed."

Since the authors found that "dumping" occurs with roughly the same frequency and severity in cases treated by different techniques of gastrointestinal anastomosis after gastric resection, they conclude that sudden distention of any part of the upper intestinal tract may produce dumping with the accompanying epigastric discomfort. They do not believe they can tell whether the epigastric fullness is due precisely to the sudden distention of the bowel or, as Welbourn (1951) suggests, to the hyperperistalsis that develops in response to this distention. Whatever the precise mechanism, the bowel in time clearly acquires a tolerance to the distention in most cases. Roentgenologically this was suggested by the finding in many cases of permanent dilatation of the duodenum or of the upper jejunum, and clinically it is reflected in the gradual diminution in the severity of the symptoms.

The authors comment on the work of Moroney (1951) on the use of a transplant of an isolated segment of transverse colon to provide a gastric reservoir after partial gastrectomy, and of Lee (1951) on the use of transposed terminal ileum, cecum, and ascending colon for the same purpose after total gastrectomy. They, themselves, have done 12 subtotal gastrectomies with implantation of a 6 inch length of transverse colon between the gastric remnant and the duodenum and 3 total gastrectomies with interposition of a similar but rather longer segment of transverse colon between the lower end of esophagus and the duodenum. In all cases the colon graft was placed antiperistaltically—*i.e.*, with the splenic flexure end to the esophagus or the stomach, and the hepatic flexure end to the duodenum. Their experience, however, has not been too encouraging. Roentgenologically there has been delay up to one and a half to two hours in the emptying of the stomach remnant and colon transplant in 4 cases. In the remaining patients treated by this method, including the 2 surviving total gastrectomy patients, emptying was rapid, as in the more orthodox gastric resections.

The article is richly illustrated with sketches of the different types of gastrectomies performed. In addition there are numerous roentgenographic illustrations of resected stomachs demonstrating the distention of the jejunal loop.—*Ralph F. Niehaus, M.D.*

Pirkey, Everett L., Reed, Edsel S., Smith, William H., and Whiteman, Gabriel. "Profile line" in roentgenologic differentiation of intrinsic and extrinsic lesions of the stomach. *J.A.M.A.*, March 29, 1952, *148*, 1095–1097.

The portions of the stomach that are not available for palpation have long offered radiologists considerable difficulty in diagnosis. The authors suggest a new method to produce controlled pressure in the stomach, above the costal margin, for better evaluation of abnormal findings.

The actual procedure consists of usual roentgenographic examination of the stomach and, if abnormalities are detected, the patient is made to swallow an ordinary stomach tube with a fresh latex condom tied to it. Once in the stomach, the balloon is inflated with varying pressures and amounts of air as needed. Intragastric pressure used never exceeded 20 mm. of mercury. Little discomfort has been noted by the patients.

After inflation of the balloon, conventional stereoscopic roentgenograms are made.

Among other roentgen signs found helpful as a result of this method, is the "profile line" which consists of a thin layer of barium sulfate trapped between the distended balloon and the smoothed-out normal mucosa. The authors noted that if the mucosa is roughened, owing to an infiltrative process, then the "profile line" is absent. The "profile line" will follow indentations caused in the stomach wall by neighboring viscera and extrinsic masses, and will also extend smoothly over extramucosal intramural tumors that have not ulcerated.

The authors feel the method is of value especially in evaluating false positive cases. Besides the "profile line," other diagnostic signs found with this method are elasticity, mobility and characteristic mucosal pattern of the stomach.—*Lawrence R. James, M.D.*

Elliott, Gladden V., and Wilson, Hugh M. Mesenchymal tumors of the stomach. *A. M. A. Arch. Int. Med.*, March, 1952, *89*, 358–367.

Leiomyomas and lymphosarcomas are the most frequent of mesenchymal tumors of the stomach, and of greatest clinical significance.

Leiomyomas show the following characteristics: Gastrointestinal bleeding is common and may account for an unexplained anemia. Ulceration is common. The roentgen findings include: a sharply circumscribed smooth intraluminal filling defect; abrupt obliteration of gastric rugae over the tumor, with normal architecture in the surrounding area; pliable gastric walls and peristaltic activity, and occasionally ulceration in the central portion of the tumor. The tumor may be best seen in a partly filled stomach. Differential diagnosis between the various mesenchymal tumors is not possible. While the criteria for benign tumors are fairly accurate, a carcinoma may give the same findings. An extra-

gastric mass may likewise produce a pressure defect and simulate an intramural tumor.

Lymphosarcomas exhibit the following picture: They may originate primarily in the stomach, or may involve the stomach secondarily as part of a generalized disease. Primary lymphosarcomas have the same age range, symptomatology and clinical findings as carcinomas. Pain, bleeding and ulceration are common. Roentgen examination is of little aid in differentiating from carcinomas as the lymphosarcomas may also give rigidity to the walls. Secondary lymphosarcomas are suspected when large gastric lesions are found in patients known to have lymphosarcomas elsewhere.—*Joseph Levitin, M.D.*

YARNIS, HARRY, MARSHAK, RICHARD H., and FRIEDMAN, A. I. Gastric polyps. *J.A.M.A.*, March 29, 1952, *148*, 1088–1094.

After defining the polyps as epithelial projections and stressing the fact that in the gastrointestinal tract they should be called adenomas because they are benign and proliferative, the authors present the details of their 73 cases and a brief review of the literature.

The incidence of adenomas, in the cases reported here, was 1.6 per cent as found by roentgen examination or gastroscopy. In 8,735 autopsies done, the incidence was 0.3 per cent. These figures are comparable with others presented in the literature.

The most common clinical findings are bleeding and abdominal pain. Achlorhydria was detected in 91 per cent of cases, and histamine anacidity was found in 45 per cent. Nine per cent had normal acidity while none showed hyperacidity.

The association of pernicious anemia and gastric adenomas has been recognized clinically for a long time, and the authors report that this has occurred in 8 per cent of their cases. Four case reports are presented illustrating the various clinical courses of patients with multiple gastric adenomas.

Roentgenologic examination shows a round, smooth, translucent filling defect with a widening and displacement of the normal rugal folds. Both sessile and pedunculated types may be encountered. Air bubbles or particles of food may cause confusion, as may the rugal folds near the greater curvature of the stomach.

The authors feel that the use of compression will clarify most confusing pictures; they have found air contrast study to be unsatisfactory. The administration of small amounts of barium for mucosal relief plus gentle compression has been adequate for the most part but occasionally the tumor will be more clearly defined in a barium-filled stomach.

The belief has long been held that malignant degeneration develops in gastric adenomas. As to whether this does occur is debatable. In the 73 cases reported here, 2 were deemed to have undergone carcinomatous change, that is 6.7 per cent.

The treatment varies widely from conservative therapy to vigorous surgical intervention, and the authors feel that management of such patients depends on symptomatology, multiplicity of lesions, and the appearance of these at gastroscopic examination.

In their series, 36 patients had gastric resection while 32 did not have resection. The ten year follow-up revealed no evidence of malignant degeneration in the non-surgically treated patients. The authors stress that the conservative therapy must be limited to patients with small, solitary adenomas with benign characteristics. Close follow-up is, of course, indicated.—*Lawrence R. James, M.D.*

BERKSON, JOSEPH, WALTERS, WALTMAN, GRAY, HOWARD K., and PRIESTLEY, JAMES T. Mortality and survival in cancer of the stomach; a statistical summary of the experience of the Mayo Clinic. *Proc. Staff Meet., Mayo Clin.*, April 9, 1952, *27*, 137–151.

This is a statistical article relative to the results of treatment of cancer of the stomach during a forty-two year period at the Mayo Clinic. The follow-up of 9,620 patients operated upon has been very thorough. Information on 98.9 per cent or more of the patients is available. The patients are analyzed from the standpoint of sex, age, hospital mortality following operation, survival rate following operation, survival rate relative to metastasis, the correlation of survival and grade of malignancy (Broders), survival in relation to free gastric acidity, survival in relation to sex, survival after operation early period and at present, and the fate of patients with gastric cancer formerly and today.

As with any purely statistical article, those interested must consult the original article. The only conclusions the authors draw relative to improving the salvage of patients with gastric carcinoma is that better methods of diagnosis must be developed and that patients and physicians must be educated to place more importance upon the early vague symptoms of the disease.—*John H. Harris, M.D.*

DUBOST, CHARLES, ALLARY, MICHEL, and OECONOMOS, NICOLAS. Resection of an aneurysm of the abdominal aorta; reestablishment of the continuity by a preserved human arterial graft, with result after five months. *A. M. A. Arch. Surg.*, March, 1952, *64*, 405–408.

This is a brief case report of the successful resection and replacement by a graft, of an abdominal aneurysm, which involved both common iliac arteries. Pre- and postoperative aortograms are shown. —*Edgar C. Baker, M.D.*

MOORE, THOMAS C. The management of intussusception in infants and children; report

of 43 cases. *Ann. Surg.*, Feb., 1952, *135*, 184–192.

The great majority of cases of intussusception in this study occurred in infants under two years of age. Thirty-six of these 43 patients were under twelve months or younger. The possible etiologic factors in this group leading to intussusception were obscure. A Meckel's diverticulum was found to be the leading point in 2 cases, and in 1 other case, the duplication of the terminal ileum was presumed to have been involved in the initiation of the intussusception. In the rest of the cases no definite etiologic factor was found. Clinical histories were remarkably uniform. Most of the patients were healthy, well nourished infants who had suffered the sudden onset of intermittent colicky abdominal pain and vomiting with the subsequent passage of bloody stools, which, when mixed with mucus, occasionally had a "currant jelly" appearance. In those cases not receiving early treatment, the picture was that of progressive, strangulated small intestinal obstruction, marked by dehydration, hyperpyrexia, abdominal distention, peritonitis, and ultimate death.

The most prevailing physical findings are limited to the abdomen and rectum. Abdominal palpation listed evidence of mass in 29 cases. The presence of gross or occult blood on the examining finger following digital rectal examination was often helpful in making the diagnosis.

Barium enema studies under fluoroscopic control were employed in 27 cases, either to substantiate the diagnosis in certain cases, or to attempt to reduce the intussusception in others. Attempts at fluoroscopic barium enema reduction of the intussusception were made in 16 cases, and were successful without operation in only 2 instances. Of the 14 unsuccessful cases subsequently operated upon, the intussusception was already reduced when the patient was explored, in 1 case, and in another case, presumably reduced intussusception by roentgen examination was still present in the cecum. It is also of interest that in this group of 14 cases 2 Meckel's diverticula and 1 duplication of the terminal ileum were discovered at operation. In only 8 of the 14 cases was the intussusception found in essentially the same location at operation as when last observed under fluoroscopic examination. In 17 attempts at non-operative reduction success without operation was achieved in only 2 cases. Of the 15 patients subsequently operated upon, 3 required major bowel resections, and 1 patient died from gangrenous perforation of the ileum, a complication which might possibly have been avoided had the patient been operated on earlier. The author emphasizes that neither vigorous, prolonged, nor repeated efforts at non-operative reduction were made in those cases in which the intussusception was not easily reduced.

When analyzing the relationship of symptom-duration to mortality, it was found that no deaths occurred in those infants treated during the initial twenty-four hours of illness, and that the mortality, thereafter, rose progressively. The mortality rate in the entire group was 18.9 per cent. In all of the patients who died the interval between the onset of symptoms and operation was prolonged, and most of these patients exhibited marked elevation of temperature on admission to the hospital. Five of the 7 infants died within five hours after completion of the operative procedure; in most cases, only reduction had been attempted.

The problems presented by intussusception in children over two years of age are somewhat different from those encountered in infants. There were only 6 instances of intussusception in children in this series, and their ages ranged from four to eighteen years. The onset of symptoms in this group was more prolonged and less dramatic than was generally experienced in the infant group. A mass was palpable on abdominal examination in 4 of the cases. Roentgen examination by barium enema was undertaken in only 1 case, and in none of the cases was an attempt made to reduce the intussusception by non-operative measures. A demonstrable leading point for the intussusception was found in 5 of the 6 cases. The etiologic cause in 2 of the cases was Meckel's diverticulum. A polypoid adenoma of the jejunum, lymphosarcoma of the terminal ileum, and multiple polyposis were the initiating factors in 1 case each. Two of the 6 patients died postoperatively—a mortality rate of 33 per cent. In 1 of the cases the patient arrived at the hospital in a morbid condition. The operative management involved simply the drainage under local anesthesia of grossly contaminated peritoneal cavity.

This paper is well worth reading in its entirety. Probably the most important point of the summary is the speed with which the intussusception is recognized and effectively treated. Unquestionably it is the most important factor in influencing the outcome of intussusception in infants and children.—*E. A. Addington, M.D.*

Byrne, John J., Swift, Charles C., and Farrell, George E., Jr. Volvulus of the cecum. *A. M. A. Arch. Surg.*, March, 1952, *64*, 378–383.

A description of a rare condition apparently derived from the literature and the roentgen findings which give a correct preoperative diagnosis are combined with a report of 3 cases. Hypermobility of the cecum with a possible fixed ileum as a point of torsion is added to inciting causes such as a high residue diet, pregnancy, violent peristalsis or even trauma of the abdomen. The signs and symptoms are those of intestinal obstruction. The roentgen examination is regarded as the best diagnostic procedure.

The typical roentgen finding "is a markedly dilated loop of cecum and ascending colon which usually assumes a transverse position in the middle or upper abdomen." There is an absence of colonic gas in the right lower quadrant. Dilated small bowel may be seen. Barium enema may be a help but is regarded as unwise.

Treatment is surgical. Cecostomy is considered as the best procedure. Three case reports are given. Two of these were diagnosed by roentgen examination.—*Edgar C. Baker, M.D.*

Berry, Robert E. L. Diagnosis and treatment of acute intestinal obstruction. *J.A.M.A.*, Feb. 2, 1952, *148*, 347–355.

This discussion is another plea for the early recognition and treatment of intestinal obstruction. The commonest causes of death in small bowel obstruction are peritonitis and infection, and these are late manifestations of intestinal obstruction.

The author points out the very great importance of differentiating strangulated obstruction of the bowel from simple obstruction. Few more positive indications for operative intervention exist than in intestinal obstructions in which the blood supply of the obstructed loop has been compromised. The article contains a well outlined chart on the differential diagnosis between strangulated and simple bowel obstruction.

The most important laboratory aid in the diagnosis of intestinal obstruction is the survey roentgenogram of the abdomen. Roentgenograms taken early after the onset of symptoms, in cases of simple obstructions, may show little, but as distention progresses the involved loops begin to lie in horizontal fashion across the abdomen, and give rise to familiar step-ladder arrangment of the coils of the distended gut. In the cases of strangulating obstructions early survey roentgenograms may be of great value. Because of the nature of these lesions, an early distended closed C-loop may stand out vividly. The presence of such an isolated loop of small bowel associated with other diagnostic features of strangulated obstruction is almost pathognomonic. As distention progresses, however, this loop may disappear in the pattern of many distended coils of bowel. The presence of fluid manifested by a hazing of the viscera is further corroborating evidence of a strangulated obstruction, provided other diagnostic features are present.

It is pointed out that vascular obstruction, mesenteric embolism and thrombosis are recognized preoperatively with great rarity. The nature of the diseased processes with which these lesions may be associated can be of help in diagnosis.

Carcinoma is by far the commonest cause of acute mechanical obstruction of the colon. Fundamental differences in the anatomy and physiology of the large and small bowel produce, however, marked variations in the clinical response to obstructions. Strangulated obstructions of the colon are not particularly common, and the majority of them are a volvulus of either the sigmoid colon or cecum.

The paper includes a generous discussion of the management of acute intestinal obstruction, both surgically and medically.—*E. A. Addington, M.D.*

Calvy, George L., and Dundon, Carroll C. Roentgen manifestations of acute intermittent porphyria. *Radiology*, Feb., 1952, *58*, 204–208.

The authors present a study of 17 patients with acute intermittent porphyria and a review of the literature. Segmental gaseous dilatation of the intestine was found in at least 50 per cent of these patients who presented symptoms of an abdominal-visceral crisis with signs of intestinal obstruction. The intestinal tract findings are attributed to scattered areas of smooth muscle spasm and intervening dilatation of the intestine with resultant pain and tenderness. These roentgenographic findings will vary from day to day.

The diagnosis of this disease is made on the demonstration of porphobilinogen (or abnormal porphyrins) in the urine and feces. The radiologist who is aware of this disease and its manifestations should mention it in the differential diagnosis of problem cases which present symptoms of obscure abdominal pain, and particularly in those cases with segmental gaseous distention of the intestine. It is also important, however, to know that the patient may have abdominal pain due to acute porphyria with a normal roentgenogram.—*Donald N. Dysart, M.D.*

Jolleys, A. Death following a barium enema in a child with Hirschsprung's disease. *Brit. M. J.*, March 29, 1952, *1*, 692–693.

It is generally recognized that barium enemas must be given with caution in cases of megacolon, because of the danger of precipitating intestinal obstruction.

The following is a case report of a male child (almost four years of age) who had been constipated since birth, and died during a convulsive seizure twenty hours after a barium enema.

Before administering the barium enema, he had been given 1 pint soap enemas daily until his bowel appeared to have been satisfactorily cleared of feces, although the abdomen was still distended. No ill effect was noted following the soap-sud enemas.

Four pints of barium emulsion were introduced, and the roentgen examination showed a typical appearance of Hirschsprung's disease with a short aganglionic segment. An attempt was made to siphon back the barium emulsion without success. On return to his bed the child collapsed and was sweating. A soap enema (1½ pints) was given, but this too was retained. About seven hours later he lapsed into

coma, became cyanosed, and began to have generalized convulsions. The child died in a convulsion twenty hours after the enema had been given.

Permission for necropsy was not obtained, but the author believes that the cause of death was due to water intoxication. He discusses water intoxication as a cause of death and cites from the literature the cases of Helwig, Schutz, and Curry (1935) and of Hiatt (1951). The symptoms of water intoxication are due to the increase in interstitial and intracellular fluid. Treatment of an established case should aim at causing a shift of this fluid back into the circulatory system.

The treatment recommended by the author is the transfusion of hypertonic saline. The amount of sodium ion that is needed can be calculated if the volume of absorbed water is known. If circulatory failure occurs, owing to a rapid increase in circulating volume, a venesection is necessary.—*Ralph F. Neihaus, M.D.*

Gynecology and Obstetrics

Riley, Gardner M., Behrman, J. S., Arcilla, Angelina, and Dontas, Eugenia. Clinical evaluation of the silver carbonate vaginal smear method in the diagnosis of uterine cancer. *Am. J. Obst. & Gynec.*, Nov., 1951, *62*, 985–996.

In 1948 one of the authors (G.M.R.)[1] reported that exfoliated cells, as found in the vaginal smear, were readily impregnated with silver carbonate solution prepared according to the method of Del Rio Hortega.[2] Of particular importance was the observation that the chromatin material was remarkably argyrophilic. Since the primary criteria for malignancy are nuclear characteristics, a distinctive nuclear stain is most desirable. The clinical experiences with this method during a three year period are reported in this article.

Not infrequently the routine procedure results in a heavy silver impregnation of the nucleus. As a result, the nucleus may present a solid, amorphous appearance for which the technique may be criticized. The intensity of the stain has served the useful purpose of attracting the examiner's eye to the suspicious cell. Although silver carbonate solution is excellent for the demonstration of such cytological details as reticular fibers and neural elements, the nuclear staining property of the solution is best demonstrated in a thin spread of exfoliated cells.

Smears were secured from patients on the gynecology service of the Department of Obstetrics and Gynecology at the University of Michigan Hospital; they were taken whenever the history, symptoms, or clinical findings were such as to suggest the possible existence of carcinoma. The most common symptom was abnormal bleeding, either irregular or seemingly of a nonfunctional nature. The ages ranged from thirteen to eighty-four years. Seventy-eight per cent of the subjects were from thirty-one to sixty years of age. Over half (58 per cent) of the subjects were in the forty-one to sixty age group. In the premenopausal subjects the most common clinical findings were hyper- and polymenorrhea, intermenstrual spotting, cervical erosion, or vaginal discharge. Smears were generally not taken in cases of clinically obvious carcinoma.

During the three year period of this investigation slides satisfactory for evaluation were obtained from a total of 2,008 patients. The total number of carcinoma cases in this series as proved by biopsies or endometrial curettements was 120. Of this number, 98 cases were correctly diagnosed, leaving a total of 22 undetected carcinomas. On the other hand, there were smears from a total of 1,888 gynecological patients in whom carcinoma was not detected clinically or pathologically. In only 22 instances were incorrect diagnoses of carcinoma reported. Thus, false positive reports were submitted in 1.16 per cent of these cases

It appears that equally as many false negative reports were obtained as false positive ones In all, a total of 44 incorrect reports were found with an overall percentage error of 2.2 per cent. Where incorrect diagnoses of carcinoma were made, no consistent explanation for these errors was forthcoming. The false positive diagnosis was most often reported in the presence of cervical erosion or cervicitis.

Fifteen or 68 per cent of the errors were attributable to failure to detect adenocarcinoma of the endometrium (10 cases) or cervical carcinoma in situ (5 cases). The 22 cases incorrectly diagnosed as carcinoma reflected the occasional inability of these examiners to distinguish between a high degree of aberration within normal limits and true malignancy.

The qualities of the stain are illustrated by photomicrographs of normal, suspicious, and malignant cells.

Improvements in methods for obtaining the cell samplings, especially from the endometrium, will tend to reduce the number of missed carcinomas.

Among the advantages of the silver impregnation technique are simplicity, rapidity, ease of examination and the facility with which nuclear aberrations are recognized.—*Stephen N. Tager M.D.*

White, Margaret Moore. Errors in technique and interpretation of hystero-salpingography and tubal insufflation. *J. Obst. & Gynaec. Brit. Emp.*, Aug., 1951, *58*, 573–582.

The author states that from an experience of over 6,750 cases submitted to tubal insufflation or hysterosalpingography, the following possible errors of technique and errors in interpretations of kymograph tracings and hysterosalpingograms have come to her notice. Errors in technique:

[1] Riley, G. M. *Am. J. Obst. & Gynec.*, 1948, *56*, 468.

[2] Del Rio Hortega, P. *Arch. histol. norm y. pat.*, 2941, 1, fasc. II, 165.

(1) Omission to take a preliminary roentgenogram of the pelvis;

(2) Failure to test for patency of the cannula prior to use;

(3) Failure to use a cannula suitable for every case;

(4) Omission to warm the opaque medium introduced;

(5) When marked angulation of the body on the cervix exists, failure to alter the position of the uterus and thereby the tubes, by affixing vulsella to the cervix, may prevent entry of carbon dioxide or fluid into otherwise penetrable tubes;

(6) In order to allow time for cornual spasm to relax and permit passage of the medium into the fallopian tubes, the opaque medium introduced into the uterus should not be allowed to escape from the cervix for two to three minutes after the roentgenogram has been taken;

(7) Great pressure should not be exerted on the barrel of the syringe used to introduce opaque medium into the uterus, unless controlled by roentgenographic screening or gross venous intravasation may occur;

(8) Use an oily preparation when making a salpingogram if there is reason to suspect previous injection;

(9) Injection of an insufficient amount of medium;

(10) Omission to take a sufficient number of roentgenograms;

(11) Failure to make a second salpingogram if the diagnosis is in doubt.

Errors in interpretation:

(1) Of tubal insufflation:

(a) To mistake intestinal borborygmi for the escape of the insufflated gas from the fimbrial end of the tube;

(b) To mistake the sound of gas bubbling through a hydrosalpinx or into a fallopian tube occluded fimbrially by adhesions for escape into the peritoneal cavity;

(c) To mistake the sound of small escapes of gas from the cervix for gas escaping from the tubes;

(2) Of the hysterosalpingogram:

(a) Wrong assessment of the size of the uterus by failure to realize that the hysterogram depicts only the cavity of the uterus;

(b) Omission of details regarding irregularity of contour of the uterine cavity;

(c) To make a diagnosis on the state of the tubes from the salpingogram alone;

(d) Omission of details regarding length, caliber tortuosity, irregular filling, etc.;

(e) To mistake opaque medium still present in the tubes for peritoneal spill;

(f) To miss the significance of localization of peritoneal spill—peritoneal pockets;

(g) To mistake other pelvic shadows for peritoneal spill such as calcified lymph nodes, residue in the vagina, etc.—*Karl K. Latteier, M.D.*

DIDDLE, A. W., and O'CONNOR, K. A. Feminizing ovarian tumors and pregnancy. *Am. J. Obst. & Gynec.*, Nov., 1951, *62*, 1071–1078.

Sterility is expected theoretically in the presence of feminizing ovarian tumors. They produce hyperestrinism that inhibits the pituitary and secondarily the remaining normal ovarian tissue. As a result, they are seldom seen among pregnant women. A summary is presented of patients with known relation between tumor and pregnancy. The study shows that these neoplasms may produce serious complications during pregnancy or preclude pregnancy.

Case reports of 1,193 women with theca (263 cases) or granulosa cell (930 cases) tumors were collected from previous communications and by personal observation. There were 37 cases, including 2 of the authors' cases, where there were sufficient data to evaluate the relation of these neoplasms to pregnancy. The age was known for 29 of these women. More than 1 in 7 were in the second decade of life, over one-third in the third decade, while the others were in the fourth and fifth decades. Parity was known for 25 women. Two out of 5 were nulligravidas or nulliparas. The remainder were either gravid or had previously been gravid.

A correct diagnosis was never made preoperatively among women with feminizing ovarian tumors coexistent with pregnancy and seldom in those with abortive tendencies or with sterility. On the contrary, the diagnosis was usually suspected by gross examination of the neoplasm on the operating table or at autopsy.

The patients with both the theca and granulosa cell neoplasms were divided into three categories, according to the relation of the symptoms and signs of pregnancy: (1) the tumor was found during pregnancy or a few days post-partum; (2) abortive tendencies antedated correct diagnosis; and (3) sterility preceded surgical intervention, which in turn was followed by pregnancy.

Thecomas were found in 8 of the 37 women. None showed evidence of malignancy. Tumor and pregnancy were coexistent in 5 women. Three out of 8 patients successfully carried their pregnancies to term with the thecomas present, but 2 of these died post-partum of intraperitoneal hemorrhage. One in 8 conceived after removal of the neoplasm. Half aborted either before or after surgical treatment. One-half of the women were well one-half to five years later, one-fourth died, and the remaining fourth were lost.

Granulosa cell tumors were found in 29 of the 37 women studied. They proved to be malignant in 5 instances; the others were benign. Pregnancy was coexistent with the tumor in 12 women. There were 12 women with antecedent sterility. After surgical treatment, 9 women conceived within two months to five years. Nearly one-half of the 12 pregnant women with tumor went to term, a fourth aborted, and the

outcome for the remaining third was unknown. After removal of the neoplasm there were 16 pregnancies among 15 women, yielding 6 viable babies, 2 nonviable fetuses, and an unknown outcome for 8 others. Nearly one-fifth of the women died, or were still living after a recurrence of the tumor. Over one-half were well without recurrence a few months to sixteen years postoperatively, and over one-fifth were lost.

In 3 of the patients with thecomas there was enough hormonal activity to produce masculinizing signs. On the contrary, not enough was present to prevent the onset of pregnancy. Expressed in percentage, the theca cell tumor was more often associated with abortive tendencies than was the granulosa cell variety.

This study revealed that a woman may have a feminizing ovarian tumor removed, bear children thereafter, and still have a fatal recurrence years later.—*Stephen N. Tager, M.D.*

Hemley, Samuel D., and Schwinger, Aaron. Lithopedion; case report and survey. *Radiology*, Feb., 1952, *58*, 235–238.

This is a report of a case of lithopedion found on roentgenographic examination in a sixty-nine year old female.

The literature is reviewed and the following classification given:

1. Lithokelyphos in which membranes alone are calcified.
2. Lithokelphopedion in which both membranes and child are calcified.
3. True lithopedion in which the fetus is calcified and calcification of membranes is negligible.

Judging from the recent literature, lithopedion is a rare occurrence.—*McClure Wilson, M.D.*

Livesay, Jackson E., Griffen, Ernest P., and Sheeran, Dan H. Bicephalic monster; case report. *Radiology*, Feb., 1952, *58*, 239–240.

This case is thought to be the first recorded instance of a bicephalic monster recognized by roentgenograms prior to delivery. This unusual development is said to be due to incomplete fission of two impregnated ova. This patient had received no previous irradiation. Delivery of the stillborn fetus was by a low cervical cesarean section. Postpartum roentgenograms of the fetus showed two heads, four arms, fusion of the thoracic cages, two spines, but one pelvis and sacrum and only two legs.—*Donald N. Dysart, M.D.*

Diddle, A. W. Granulosa- and theca-cell ovarian tumors: progonosis. *Cancer*, March, 1952, *5*, 215–228.

The author collected 1,189 cases of feminizing ovarian tumors from the literature. (A comprehensive bibliography of 277 references is included in the article.) Thirty-five of these neoplasms were personally studied. Although a statistical analysis could not be made because of incomplete follow up studies, the material did lend itself toward pointing out criteria of prognostic value in estimating the outcome for women with either granulosa-cell or theca-cell tumors.

Total hysterectomy with bilateral salpingo-oophorectomy is recommended as the treatment of choice in older patients. During prepubertal and reproductive periods of life, less drastic surgery may be used if the neoplasm is well encapsulated.

Both of these feminizing tumors are usually radiosensitive. When metastases are present, palliative irradiation is advisable. It is doubtful that cures can be obtained by irradiation alone.

The five year survival rate does not necessarily indicate a cure and does not bear the same evaluation as in some other forms of cancer. In the cases that could be followed, one-third of the recurrences were noted after five years and one-fifth after ten years.

These studies also demonstrated that the combination of feminizing ovarian tumors and uterine cancer is not unusual. It was estimated that the incidence of endometrial carcinoma was one hundred times greater in the presence of these neoplasms than in their absence. Uterine cancer is found more often with the theca-cell than with the granulosa-cell tumors.—*Russell Wigh, M.D.*

Genitourinary System

De Gouvêa, Gustavo Soares. Refluxo espontâneo durante a urografia excretória. (Spontaneous reflux during excretory urography.) *Rev. brasil. de cir.*, Nov., 1951, *22*, 307–314.

In a man, aged sixty-five, with massive spontaneous asymptomatic hematuria of the right kidney, extensive reflux of the contrast medium into the perirenal tissue was noted after intravenous injection of uroselectan B. Similar reflux occurred, though less pronounced, after retrograde pyelography. Otherwise the roentgen appearance of the kidneys and the ureters appeared normal. In view of the massive hematuria, the diagnosis of renal tumor was made and nephrectomy was performed. Macroscopically, no tumor could be demonstrated, and only with difficulty a small nodular lesion could be ascertained which microscopically was shown to represent an early clear cell carcinoma of the renal papilla.

The different possibilities of renal reflux (tubular, lymphatic, interstitial and venous) are discussed in detail. In the absence of renal blockage, of increased intrarenal pressure or of any history of traumatism, it is assumed that the reflux was lymphatic in character.—*Ernst A. Schmidt, M.D.*

SWENSON, ORVAR, MACMAHON, H. EDWARD, JAQUES, WILLIAM E., and CAMPBELL, JAMES S. A new concept of the etiology of megaloureters. *New England J. Med.*, Jan. 10, 1952, *246*, 41–46.

Autopsy material of 7 test cases with findings of megalobladder and megaloureter were compared with 9 control cases. The studies show a diminution of parasympathetic ganglion cells in the bladder of the test cases and this may be the fundamental change in the megalobladder associated with Hirschsprung's disease.

Megaloureters are primarily the end result of a long standing malfunctioning bladder and usually have a free reflux from the bladder.—*Allison E. Imler, M.D.*

NELSON, O. A., and MOUSEL, L. H. Renal tumors. *J.A.M.A.*, Jan. 19, 1952, *148*, 171–174.

The authors advocate the use of arteriography as the most valuable diagnostic procedure in cases of suspected renal neoplasm.

Nephrectomy is the recognized treatment for renal tumors.

Replacement of blood loss and careful anesthetic management reduces morbidity and mortality.

Radiation therapy should not be utilized as the primary method of definitive treatment. The value of preoperative and postoperative irradiation has not been settled.—*Allison E. Imler, M.D.*

JEWETT, HUGH J. Infiltrating carcinoma of the bladder; relation of early diagnosis to five-year survival rate after complete extirpation. *J.A.M.A.*, Jan. 19, 1952, *148*, 187–189.

The author surveys a total of 73 cases of bladder cancer with particular reference to the depth of invasion and its influence on the prognosis. Complete removal of the superficially infiltrating cancer results in a five year survival rate of 74 per cent. When invasion extends more than halfway through the muscularis, the five year survival rate is only 3 per cent.

Late or neglected symptoms together with inadequate treatment after early diagnosis permit tumor cells to extend deep into the bladder wall. Early diagnosis and complete removal of the superficially infiltrating bladder cancer can result in a marked improvement in the over-all five year survival rate.—*Allison E. Imler, M.D.*

SILVERMAN, FREDERIC N. Urologic problems in pediatric x-ray diagnosis. *Radiology*, March, 1952, *58*, 325–337.

The failure to grow, the presence of an abdominal mass, and clinical sign of urinary system abnormality are the most common indications for roentgen examination of the urinary tract in infants and children. The same diagnostic procedures are employed in children as in adults.

A complication frequently observed in children with the clinical manifestations of pyelonephritis is penetration of renal parenchyma by the catheter or contrast medium during retrograde pyelography. Since the normal renal pelvis can withstand considerable pressure and distortion, this is thought to indicate sites of inflammatory reaction.

The diagnosis of neurogenic uropathy should not be made on the basis of spina bifida occulta unless a neurologic defect can be demonstrated. Adequate studies have not been made of intramural neural elements in so-called neurogenic ureteral disease.

The diagnosis of ureterocele, ectopic ureteral orifices and posterior urethral valves is discussed and the differential diagnosis of Wilms' embryoma, neuroblastoma and hydronephrosis is developed.—*Arno W. Sommer, M.D.*

ROSS, JAMES A. Studies in pyelorenal backflow. *Brit. J. Urol.*, March, 1952, *24*, 27–38.

The author describes an investigation which was carried out, consisting of (1) review of clinical case histories and roentgenograms, and (2) injections and dissections of cadaver kidneys, to reproduce, if possible, the appearances noted roentgenologically and so determine their nature.

The case records of 1,876 patients—883 males and 993 females—were reviewed. In 38 of these cases, *i.e.*, in 2 per cent, some degree of pyelorenal backflow was noted.

Different types of pyelorenal backflow occur such as the pyelo-interstitial or pyelosinous, pyelovenous, pyelotubular or pyelocanalicular, and the pyelolymphatic or sinolymphatic types.

The author concludes that he has not determined exactly what produces the appearance of the fine lines and streaks passing medially from the kidney in certain retrograde pyelograms. This may be due to pyelolymphatic backflow but some of the wider channels may represent pyelovenous backflow.

Experiments carried out on cadaver kidneys show that it is as easy to inject the veins via the ureter as via the main renal vein. Good examples of pyelovenous backflow were obtained in readily demonstrable form, as neoprene casts. Casts and histological evidence of lymphatic channels have not as yet been obtained. The author states that it seems likely that the usual sequence is pyelo-interstitial extravasation with a combination of pyelovenous and pyelolymphatic backflow, both of which produce the appearances seen on the roentgenograms.

Excellent illustrations are presented.—*C. Peter Truog, M.D.*

BERRY, N. E., WHITE, E. P., and METCALFE, J. O. Abdominal aortography in urology. *Canad. M. A. J.*, March, 1952, *66*, 215–217.

The authors regard aortography as a simple and

safe procedure when urokon is used. The technique as described is simple.

A 12 cm., 18 gauge needle is connected by a 6 inch piece of rigid tubing with a 20 cc. syringe. The needle is inserted below the left 12th rib three to four fingers breadth from the midline. It is advanced forward, upward and medially to the body of the 12th thoracic vertebra. The needle is withdrawn and then moved forward to slide in front of the vertebra and into the aorta. The contrast medium (10–20 cc.) is injected in about three seconds and a film exposed immediately. A second film two seconds later gives an excellent nephrogram. Later films give excretory urograms.

The authors feel that the method is simpler than doing a pyelogram. They regard the vascular pattern obtained of great value.—*Edgar C. Baker, M.D.*

Wilhelm, H. Die Hydrocele renis, ein Krankheitsbild oder ein Symptom? (Hydrocele of the kidney, disease entity or manifestation?) *Chirurg*, March, 1952, *23*, 111–115.

Large accumulations of fluid between the capsule of the kidney and kidney surface have been described very seldom. In the literature, this condition has been designated under several names: perirenal hydronephrosis, perirenal hygroma, hydrocele of the kidney, etc. Since at operation and upon histopathological studies, this condition simulates so much a hydrocele of the testicle, the term hydrocele of the kidney is considered to be most appropriate. The condition consists of a cyst bordering upon the kidney parenchyma and the elevated capsula propria.

A case report of a thirty-four year old individual is presented. The patient noticed sudden sharp pain in his left loin, followed by a swelling over the left abdomen several days later. Intravenous urography showed a large round mass in the left abdomen. At laparotomy, a retroperitoneal cystic tumor containing 2,500 cc. of clear, yellow fluid was found and drained. The cyst refilled in three days. Re-operation found the mass to be as large as before. In the depth of the cystic sac, the kidney was found, from the lower pole of which there was a fibrous strand running to the posterior portion of the wall of the cyst. The wall of the cyst was removed from the hilus of the kidney. About six weeks after this operation, a cystic tumor was felt in the right upper abdomen. Intravenous pyelography now showed a mass on the right side similar to the one noted previously on the left. Operation was then performed and the cyst of the right kidney was removed.

The various theories regarding the cause of hydrocele of the kidney are discussed. Review of previously published cases shows that puncturing of the cyst is of temporary benefit, since these cysts refill in a few days. Morphological changes in the kidney have not been described. Urinary findings are usually normal, although occasionally there is a small amount of albuminuria. The concentration of the kidneys is either normal or diminished slightly. Intravenous urography shows the ureter to be displaced mesially. The calyces of the kidney are normal, in contrast to the findings seen in the so-called kidney cyst in which they encroach upon the kidney parenchyma. In the author's case, there was a marked hypertension; the blood pressure findings are not mentioned in the other published cases.

The author believes that hydrocele of the kidney is not a disease entity, but is a manifestation of "serous" chronic nephritis. This conclusion is based upon the presence of hypertension and the nature of the transudate type of fluid found in the cyst. Regarding treatment, author believes that the capsule of the kidney should be removed as much as is possible technically. Nephrectomy should not be done because of the danger of bilateral occurrence of the cyst.—*Samuel Richman, M.D.*

Lewis, Evan L., and Kimbrough, James C. Megalo-ureter; new concept in treatment. *South. M. J.*, March, 1952, *45*, 171–177.

The term megalo-ureter was first used by J. R. Caulk in 1923 who in reporting the condition expressed the opinion that it was caused by the presence of ureteral valves. Many writers have since then described the neurogenic megalo-ureter.

The syndrome exemplifies the following points: (1) dilated ureter, either unilateral or bilateral; (2) no evidence of true obstruction; (3) the pelvis and calyces are not dilated in proportion to the ureter; (4) peristalsis present in the dilated ureter; (5) there is a normal undilated segment at the lower end of the ureter varying in length from a few millimeters to several centimeters. Hydroureter due to obstruction must always be differentiated.

What is the cause of this syndrome? It is thought to be similar to megalo-esophagus, cardiospasm or megacolon.

Treatment consisted of nephro-ureterolysis in 3 cases observed by the authors. Symptoms were relieved in 2 cases. Other methods of treatment suggested are: presacral neurectomy, nephrostomy, cystostomy and nephroureterectomy.

Several case reports and photographs are given.—*Robert J. Reeves, M.D.*

Moore, Thomas. Ectopic openings of the ureter. *Brit. J. Urol.*, March, 1952, *24*, 3–18.

The author gives an excellent discussion on the embryology of the ureters, kidney and bladder.

The incidence of the anatomical types of ectopic ureters as reported by Moore (1948) in 185 cases is as follows:

1. Complete unilateral duplication of pelvis and ureter with an ectopic opening of the super-

numerary ureter, 96 cases (51.9 per cent). (Author—5 cases.)
2. Single ureter with ectopic opening, 58 cases (31.5 per cent). (Author—1 case.)
3. Bilateral duplication of pelves and ureters with one ectopic opening only, 21 cases (11.4 per cent).
4. Both single ureters having ectopic openings, 6 cases (3.2 per cent). (Author—1 case.)
5. Complete unilateral duplication of pelvis and ureter with ectopic openings of both ureters, 2 cases (1 per cent).
6. Bilateral duplication of pelves and ureters with bilateral ectopic openings, 2 cases (1 per cent). (Author—1 case.)
7. Supernumerary kidney, pelvis, and ureter with an ectopic opening, 0.

The author discusses the clinical types according to site of implantation of the ectopic ureter and the sex of the patient.

1. Intravesical ectopia—both sexes.
2. Extravesical ectopia
   (a) Male—no incontinence.
   (b) Female—incontinence in addition to normal control at regular intervals.
3. Bilateral supernumerary intra-urethral ureters.
4. Ectopic accessory ureter joining the vagina.
5. Ectopic accessory ureter joining the vestibule —incontinence.

Cases of each type are presented.—*C. Peter Truog, M.D.*

Adams, A. Wilfrid. Ureteric compression by traction diverticulum of the duodenum. *Brit. J. Urol.*, March, 1952, *24*, 19–22.

The author describes 2 cases in which a constriction of the right ureter was found to be due to a traction diverticulum of the duodenum which extended from the junction of the second and third parts of the duodenum across and laterally to an apex beyond the right ureter which was acutely constricted by a peri-ureteric fibrosis. There was a hydronephrosis and hydroureter proximal to the constriction. The constriction was some 2 inches below the pelvi-ureteric junction. In both cases there was an antecedent history of bilateral renal infection and in both cases the left kidney had been previously removed. Subsequently, a chronic perinephritis with inflammation of Gerota's sheath had implicated the convex border of the duodenum and led to the development of a fibrous cone which constricted the right ureter.

Treatment was surgery in which the fascial bands were cut. This was followed by adequate renal excretion and ureteric drainage.

Illustrations show the stricture of the ureter but there are no illustrations showing the diverticulum of the duodenum. Apparently the traction diverticulum mentioned is not the cause of the ureteral constriction but a result.—*C. Peter Truog, M.D.*

Nervous System

Luke, Josephus C. The costobrachial syndrome. *Canad. M.A.J.*, Feb., 1952, *66*, 127–131.

The author defines the costobrachial syndrome as that group of neurological symptoms in the shoulder, arm, and hand with associated deranged circulation to the upper extremity which forms a definite organic entity. He subdivides the group into the following four varieties: (1) scalenus anticus syndrome; (2) cervical rib; (3) costoclavicular syndrome; and (4) hyperabduction syndrome. The author emphasizes that the points of compression at the base of the neck are located: (1) where the brachial plexus and subclavian artery pass between the anterior and medius scalenus muscles; (2) to a lesser extent where the nerves and vessels pass beneath the arch formed by the coracoid process of the scapula and the insertion of the pectoralis minor muscle; and (3) also where the neurovascular structures cross the narrow space beneath the clavicle and over the first rib.

(1) The scalenus syndrome consists primarily of sensory changes in the neck and arm. These include pain and diminution of sensation and motor power in the arm with varying degrees of vascular compression leading up to gangrene and ulceration of the finger tips. This is much the same pattern as seen with a cervical rib but no cervical rib is demonstrated on the roentgenogram. A positive Adson test is very helpful as confirmatory evidence for a diagnosis of the costobrachial syndrome. An additional point is local tenderness to pressure over the insertion of the scalenus anticus muscle into the first rib. Occasionally auscultation over the subclavian vessels reveals a bruit which indicates local narrowing of the artery. This is accentuated by a downward pull of the shoulder girdle and disappears on elevation of the shoulder. Treatment of the scalenus anticus syndrome is surgical with section of the muscle at its insertion; where marked vascular signs are present, a dorsal sympathectomy with removal of the stellate and first and second dorsal ganglia is recommended.

(2) When cervical ribs are present, about half of the patients have symptoms resembling those encountered in the scalenus anticus syndrome except that they tend to appear in middle life. The author presumes this is secondary to occupation and loss of tone of musculature of the shoulder girdle with accentuation of the compression on the point causing symptoms. Surgical treatment consists in division of the scalenus anticus muscle. Occasionally a portion of the cervical rib has to be resected. One-fourth of the cases will respond to conservative management.

(3) In the costoclavicular compression the evidence of partial venous obstruction in the extremity is useful in making a differential diagnosis from the cervical rib and scalenus anticus syndrome. Usually, the superficial veins are engorged and the hands have

a cyanotic tinge. Also, venography will show a pinching of the vein at the level of the first rib. This syndrome is often associated with congenital abnormality of the first thoracic rib, which is either bifid or considerably broadened. The treatment in these cases is primarily conservative with a change in occupation and strengthening of the muscles of the shoulder girdle. Surgical treatment is difficult, requiring a section of the clavicle for adequate exposure. Occasionally in costoclavicular compression there is acute axillary vein thrombosis.

(4) In the hyperabduction syndrome the point of compression of the neurovascular structures is located beneath the coracoid process of the scapula against the attachment of the pectoralis minor. This syndrome is seen chiefly in patients who sleep with the arms over the head or those whose occupations require the arms above the head for long periods. The treatment simply consists of preventing the excessive abduction either by change of occupation or sleeping position.

The author emphasizes that careful clinical and roentgenological studies are necessary to make a differential diagnosis of the costobrachial syndrome from Raynaud's disease, Buerger's disease, herniated cervical discs, neuritis secondary to vitamin deficiencies or diabetes, coronary artery disease and lesions of the shoulder.—*T. D. Allison, M.D.*

Love, J. Grafton, and Dodge, Henry W., Jr. Dumbbell (hourglass) neurofibromas affecting the spinal cord. *Surg., Gynec. & Obst.*, Feb., 1952, *94*, 161–172.

Sixty dumbbell neurofibromas which affected the spinal cord and adjacent paraspinal structures have occurred in approximately 1,000 neoplasms of the spinal cord at the Mayo Clinic since 1914. Analysis of these 60 cases has been made by the authors.

Characteristically the spinal part of these tumors caused symptoms of cord compression when they occurred in the thoracic portion. At the lumbar and lumbosacral levels of the cord the symptoms were those of progressive failure of a nerve root. At the cervical level the symptoms were often those of a combination of root failure and compression of the spinal cord.

The symptoms produced by the extraspinal portion of the tumors varied with the level of the lesion and the nature of the paraspinal structures affected. Dumbbell tumors occurred most frequently on the dura mater and through the intervertebral foramen.

The most common roentgen evidence of the dumbbell tumor was an enlarged eroded intervertebral foramen. In 40 of the 60 cases there were roentgenographic findings of some sort. Findings other than the enlarged foramen included: erosion or shortening of the pedicles; increase in interpedicular distance; erosion of vertebral body; erosion of laminae; destruction of spinous process; decalcification of transverse process; erosion of vertebral portion of ribs; paraspinal mass; calcification of tumor; intrathoracic tumor; scoliosis; kyphosis; hydrothorax.

Examination of the cerebrospinal fluid frequently revealed incomplete or complete obstruction of the subarachnoid spinal fluid pathways with more than 100 mg. of protein per 100 cc. of spinal fluid.

Pathologically all of the tumors were neurofibromas. Malignant degeneration occurred in 1 case and questionably in a second case. It is interesting to note that from the year 1914 until the end of 1950 approximately 1,000 spinal cord neoplasms of all kinds have been operated on at the Clinic and of this number 29 per cent were neurofibromas. In most of the series reviewed by the authors, the neurofibroma was found to be the most common tumor affecting the spinal cord.

All of the tumors studied were amenable to surgery. Most of the dumbbell neurofibromas affecting the spinal cord lent themselves to one stage removal; others required two stage procedures. Removal of some of these tumors may require a qualified thoracic, abdominal, or pelvic surgeon in addition to the neurosurgeon.

The average follow-up period after operation was seventy-seven months. Dumbbell neurofibromas (neurilemmomas) were found to be extremely benign. Prognosis for recovery after complete removal of the tumor is excellent.—*Mary Frances Vastine, M.D.*

Radner, David B., and Snider, Gordon L. Recurrent laryngeal nerve paralysis as a complication of pulmonary tuberculosis; a report of two cases. *Am. Rev. Tuberc.*, Jan., 1952, *65*, 93–99.

The association of bronchogenic carcinoma and pulmonary tuberculosis and the infrequent paralysis of the recurrent laryngeal nerve by tuberculous involvement of the mediastinum make the reporting of 2 additional cases important.

In each of the present cases paralysis of the left recurrent laryngeal nerve occurred as a complication of chronic pulmonary tuberculosis of longer than ten years' duration. In both, a dense mass developed in the region of the aortic arch. Apical retraction of the left upper lobe bronchus was a factor.

Recurrent laryngeal nerve paralysis is 15 times more frequent on the left than on the right side. The left recurrent laryngeal nerve passes through a tight triangle bounded by the aorta, ligamentum arteriosum and the pulmonary artery. Not infrequently a lymph node of the tracheobronchial group is found in the triangle adjacent to the recurrent laryngeal nerve. The right recurrent laryngeal nerve is in contact with the cervical pleura only.

Tuberculous etiology is a factor in the paralysis of the recurrent laryngeal nerve in these 2 cases.—*Edward Julien, M.D.*

Alexander, F. A. Duncan, and Lovell, B. K. Roentgenologic control of nerve blocks; use of iodopyracet injection (diodrast®). *J.A.M.A.*, March 15, 1952, *148*, 885–886.

The authors advocate the injection of a contrast medium prior to use of phenol and alcohol in nerve blocks for control of pain. In a study of 710 patients they have increased the accuracy of injection and efficacy of such blocks.

Prior to this, plain roentgenographic study of needle position was utilized in 1,124 patients. Thirty-five per cent iodopyracet (diodrast) was preferred because of its physical similarities to the most commonly used anesthetic solutions. Initially, the patients were tested for sensitivity to the medium; but this was discontinued and no untoward effects were observed in the 710 patients.

The technique advocated consists of inserting the needles without anesthetic while the patient is on the roentgenographic table. The position of the needles is then checked by appropriate films. If the position seems correct a local anesthetic is injected and if, in ten to fifteen minutes, the pain is relieved, an equal volume of the contrast medium is injected. Roentgenograms are again made and the distribution of the medium assessed. If this is distributed in the desired area, the correct amount of 6 per cent phenol solution or absolute alcohol is injected after waiting at least fifteen minutes.

The authors found this procedure most helpful in blocks of the sympathetic ganglionated chain, splanchnic nerves, paravertebral and lumbar somatic blocks, and suprascapular blocks. It is not suggested for cranial nerve blocks, and is of little value in peripheral nerve blocks.—*Robert L. Raphael, M.D.*

Cossa, Paul; Martin, Lombard; Hemmi; and Ducos. Révision du syndrome de Mills. (Re-evaluation of Mill's syndrome.) *Presse méd.*, March 26, 1952, *60*, 419–420.

The syndrome described in 1899 by Mills (a Philadelphia neurologist who died in 1931) is known as ascending hemiplegia in the American literature and called progressive ascending spinal paralysis by the French. As its name implies, it is a slowly progressive hemiparalysis, ascending gradually from the foot to the shoulder in the course of several years. It may affect the opposite side after a long interval. It has hitherto been regarded as a disease of the spinal cord, first, because of its slow progression; second, because of the absence of localizing cerebral signs or symptoms.

Reviewing 14 cases recorded in the literature and 6 cases of their own, the authors found 4 instances of facial paralysis, 2 of speech difficulties, and muscular atrophy of the neck, tongue, masseter and vocal cord in other isolated instances. They believe, therefore, that the disease extends beyond the cord and involves the brain.

No roentgen examinations on patients with Mill's syndrome have been reported in the past. The authors performed encephalographic studies on 5 patients. In 4 of them, definite cortical atrophy was present, with dilated ventricles, predominantly on that side and region which corresponded to the oldest lesion of the patient clinically.

The authors conclude that Mill's syndrome is of cerebral origin, caused by degenerative atrophy of the brain, and produced not merely by physiologic senile aging but by a premature exhaustion of the native vitality of the nerve cells.

The article contains reproductions of encephalograms and brief case abstracts.—*Albert Oppenheimer, M.D.*

Murphy, Edward S., Lipscomb, William R., and Bouslog, John S. Neurogenic sarcoma treated by surgery and radiotherapy. *J. Neurosurg.*, March, 1952 *9*, 214–218.

The authors report a case of "neurogenic sarcoma"—a tumor arising from mesodermal elements of a nerve trunk in the region of the knee joint.

A detailed history and clinical summary are included along with the autopsy findings.

The primary lesion and the metastatic foci were treated by surgical excision and roentgen therapy. It is unusual that the tumor responded temporarily to relatively small doses of roentgen rays.—*Vernon L. Peterson, M.D.*

Skeletal System

Sarnat, Bernard G., and Gans, Benjamin J. Growth of bones; methods of assessing and clinical importance. *Plast. & Reconstruct. Surg.*, Feb., 1952, *9*, 140–160.

The authors review the various methods of assessing bone growth, discussing each briefly.

They point out that anthropometric measurements of the living subject are not highly accurate because of the soft tissues, but do demonstrate rate, amount, and direction of growth in an individual; whereas study of the dried specimen, while highly accurate, introduces the disadvantages of posthumous distortions and the necessity of the static cross-sectional examination of large numbers of bones of various ages.

Implantation of screws, pegs, or wires near growth centers combined with serial roentgenography is useful in determining site, rate, direction, and amount of growth. Vital staining of living bone may be accomplished by feeding madder or by intraperitoneal or intravenous injection of a 2 per cent solution of alizarine red S. These two methods are obviously applicable to experimental study only.

The histological examination of tissue preparations is a useful method and the inestimable value of impressions, casts, photographs, and roentgenograms for study and record is obvious.

With the advent of the radioactive isotopes, radioautographs have yielded considerable information on the growth and development of animals, and the possibilities of this method are far from exhausted.

The investigator will find that, in application to clinical problems, all methods are useful and necessary. The plastic surgeon particularly profits from additional knowledge concerning bone growth.—*George Cooper, Jr., M.D.*

Pease, Charles N. Local stimulation of growth of long bones; a preliminary report. *J. Bone & Joint Surg.*, Jan., 1952, *34-A*, 1–23.

In this paper 7 cases are reported in which operations were performed for local stimulation of bone growth in long bones. The cases had follow-up studies ranging from six months to twelve years. In 5, the deformity was due to poliomyelitis, in 1 to congenital hypoplasia and in one to congenital dislocation of the hip associated with hypoplasia of the femur. A secondary operation was performed in 2 cases, five and three years after the initial procedure.

The operation consisted of insertion of ivory or metal screws in the tibia and/or the femur. In all cases stimulation of growth followed operation to a variable degree. No severe deformities occurred. Included in the study are some interesting observations on the behavior of the bones in which the screws were placed. The screws were put in parallel and in practically all cases horizontal, most of them extending to or through the cortex. After remaining in a parallel position for a period of two or three years, a crossing of the screws sometimes occurred, the growth at the head of one being more rapid than the head of its partner. The author believes this affords definite proof of differential growth. Another interesting observation was that oftentimes there was an increase in the transverse diameter of the bone in the region between the screw and the epiphyseal plate. This was presumably due to resistance of the metal to the normal soft-tissue pressure against the bone, in addition to the expected increase in the transverse growth resulting from stimulation.

The author believes it is encouraging to have definite acceleration of bone growth in 4 cases of poliomyelitis occurring respectively at three, four, five and six years after onset of the disease, coincident with growth-stimulating procedures. This suggests that the cells in the cartilage columns of the epiphyseal plates have not undergone degenerative changes during these periods. Although ivory is used almost exclusively for bone growth stimulation, Pease gives a word of caution concerning the use of metals. Reports of experiments in animals have indicated that certain metals are toxic, notably magnesium.—*Ralph S. Bromer, M.D.*

Dennison, Wallace M. Unilateral limb lengthening associated with haematogenous osteitis in childhood. *Arch. Dis. Childhood*, Feb., 1952, *27*, 54–59.

Increase in girth of a long bone following pyogenic inflammation is well known. However, little of the recent literature describes an increase in length following prolonged bone infection. In a recent series of 100 cases of acute hematogenous osteitis treated with penicillin, the disease affected a long bone on 84 occasions. Measurable increase in length of the affected limb occurred in 20 cases.

An increase in length of the lower limb was noted in the following conditions seen in one unit of the Royal Hospital for Sick Children, Glasgow, during the past five years: (1) a 2 cm. lengthening after simple transverse fracture of the femur; (2) a 3 cm. lengthening associated with a diffuse angiomatous condition of one leg (congenital arteriovenous fistula); (3) a 2 cm. lengthening after recurrent hemarthrosis of one knee in a child suffering from hemophilia; (4) a 2.5 cm. lengthening after severe lacerations of the thigh and calf; (5) a 2.5 cm. lengthening in a child suffering from synovial tuberculosis of the hip; and (6) a 3 cm. lengthening associated with congenital neurofibromatosis (biopsy revealed plexiform dilatation of veins). In all these conditions, a common factor of increased blood supply was present.

The hyperemia, caused by the presence of an infected sequestrum, presumably affected the soft tissues and increased the blood supply throughout the segment. The increase in length varied from 1 to 3 cm. The lengthening usually became obvious eight to twelve months after the onset of the disease. The patients were all under thirteen years of age at the time of onset of the infection.

Sterile sequestra are usually absorbed. An infected sequestrum unless extruded must be removed surgically.

The growth stimulus, over-activated by the increased blood supply, gradually passes off. In the actively growing child a moderate increase in length (up to 2 cm.) is rectified within five years. In a series of cases of osteitis treated before the introduction of chemotherapy and followed up until adult life (10–15 years later) an increase in length of 3 cm. noted between 1936 and 1940 was no longer present in 1950. Presumably growth ceases earlier in the overgrown limb.

The growing child can compensate for a long lower limb by such postural defects as scoliosis and genu valgum. Constant watch must be maintained as such deformities develop insidiously over a period of years if suitable raising is not applied to the footwear of the normal leg.—*Stephen N. Tager, M.D.*

Kanof, Abram. Ehlers-Danlos syndrome: report of a case with suggestion of a possible causal mechanism. *A.M.A. Am. J. Dis. Child.*, Feb., 1952, *83*, 197–202.

In this paper a typical case of Ehlers-Danlos syn-

drome is reported. The patient had the following symptoms, signs and laboratory findings which may also be observed in patients with adrenal hyperadrenocorticism: (a) dermatorrhexis; (b) poor fibroblast response to subcutaneous injury; (c) fragile blood vessels; (d) weakness; (e) osteoporosis; (f) delayed epiphyseal development; (g) high normal or slightly increased excretion of 17-ketosteroids in the urine; (h) increase of the uric acid to creatinine ratio in the blood; and (i) eosinopenia.

Roentgenograms are shown demonstrating the extreme flexibility of the elbow joint, retarded epiphyseal development and osteoporosis.

One of the most striking signs of the completely developed Ehlers-Danlos syndrome is extreme fragility of the skin (dermatorrhexis). Not only is the fragility of the skin outstanding, but also the great difficulty these patients experience in healing even the smallest cuts and bruises. A marked delay or absence of fibrous tissue formation, so that eventually the wound is covered by epithelium giving rise to the fragile, papyrus-like scars, has been described by various authors.

A possible relationship between hyperadrenocorticism and Ehlers-Danlos syndrome is suggested by the author.—*Ralph S. Bromer, M.D.*

AITKEN, ALEXANDER P., and MAGILL, H. KELVIN. Fractures involving the distal femoral epiphyseal cartilage. *J. Bone & Joint Surg.*, Jan., 1952, *34-A*, 96–108.

Fractures involving the distal femoral epiphyseal plate are uncommon. In their study of cases seen at the Boston City Hospital, 15 were found out of a total of 5,500 fracture admissions in the past five years. Nine patients were followed from one to eight years. In 7 all epiphyseal cartilages had fused. All the fractures were of the avulsion type. Displacement was noted originally in any direction. Most of the fractures occurred in males between the ages of thirteen and seventeen years. In the older age group all fractures were the result of football accidents and all were seen in the autumn months.

In only 2 cases was anatomical position maintained. The fractures were divided into three types. Type I consisted of avulsion type of fracture due to the pull of attached ligaments. The entire epiphyseal plate was stripped off the diaphysis similar to stripping up a layer of plywood. In Type II, the fracture commonly involved the distal tibial epiphysis and only rarely the distal femoral epiphysis. It was a compression type of fracture with the fracture line emerging between the bony epiphysis and the epiphyseal plate without damage to the latter. In such cases growth disturbance will not occur. If, however, the fracture line crosses the epiphyseal plate and emerges between it and the diaphysis, then deformity will occur. Type III fracture was of the compression type in which the epiphyseal plate had been crushed between the bony epiphysis and the diaphysis. Deformity was anticipated following this type of injury.

The authors call attention to the role played by the medial head of the gastrocnemius in fractures with posterolateral displacement. Such fractures must be immobilized with the joint in extension, in contradistinction to supracondylar fractures which appear to be similar but require immobilization with the joint in flexion for the maintenance of reduction.

Shortening due to either premature ossification or retardation of growth or both occurred in 3 patients but in only 1, however, was it of potential clinical significance. The knee joint showed slight loss of flexion in 4 patients; slight hyperextension was present in 3 patients; an unexplained relaxation of the anterior cruciate ligament occurred in 4 patients.—*Ralph S. Bromer, M.D.*

KLINEFELTER, EDMUND W. The anomalous hyoid; review of the literature and report of a case. *Radiology*, Feb., 1952, *58*, 224–227.

A case is reported in which an anomalous hyoid bone was associated with elongated styloid processes and ossifications in the stylohyoid and hyothyroid ligaments. The reported case, a male aged thirty-nine, gave a long history of recurrent attacks of pain in the right side of the neck radiating to the external occipital protuberance. A sudden twist of the head or resting on the right side of the neck initiated the attacks. Roentgen study showed the body of the hyoid bone about 50 per cent larger than usual. The combined length of the styloid process and ossified stylohyoid ligament was 6.5 cm. bilaterally.

Although only 2 case reports were found in the literature regarding hyoid anomalies, it is suggested that roentgen study of the hyoid bone is indicated in the presence of unexplained dysphagia.—*Arno W. Sommer, M.D.*

MINAAR, A. B. DEVILLIERS. Congenital fusion of the lunate and triquetral bones in the South African Bantu. *J. Bone & Joint Surg.*, Feb., 1952, *34-B*, 45–48.

Twelve cases of congenital fusion of the lunate and triquetral bones were found by the author in South African Bantu patients. The fusion occurs in four forms: an incomplete "pseudarthrosis," bony fusion with a dividing notch at one or both surfaces, and a complete compound bone with or without other carpal anomalies.

The anthropological significance of this anomaly has been the subject of interesting speculation. It may represent an advance towards specialization of the hand, or it may signify an attempt to stabilize the post-axial border of the hand, in which case it is a primitive adaptation which has persisted.—*Ralph S. Bromer, M.D.*

Jenkins, S. Aubrey. Spontaneous fractures of both first ribs. *J. Bone & Joint Surg.*, Feb., 1952, *34-B*, 9–13.

The case reported in this paper is that of a youth aged sixteen, who when lifting a box weighing 70 lb. from the floor on to a high counter, suffered sudden pain behind the right clavicle, radiating into the shoulder and upper chest. The pain persisted as a dull ache with intermittent acute stabs when coughing, sneezing or breathing deeply. It was increased by using the right arm and especially when lifting it to shave or to drink. Roentgenograms showed a transverse fracture of the first rib in the region of the scalene tubercle. A second roentgen examination, a week later, which included both ribs, demonstrated the fracture site in the right rib more clearly than on the first examination and the left rib unexpectedly showed a large mass of callus with an irregular fracture line running transverely through it. The fracture of the left rib was symptomless and the patient could not recall any incident, injury or symptoms relating to it. A small, bony, painless swelling could be felt at the root of the neck on the left side, lying immediately behind the lateral margin of the sternomastoid muscle at its insertion into the clavicle. This was evidently the callus around the old fracture of the first rib.

Final roentgenograms, taken four months after the onset of symptoms, showed a fully developed pseudarthrosis of each fracture site. The patient had continued without symptoms at full heavy work. Thus, the evolution from a previously intact rib through the stage of a "linear" crack to pseudarthrosis was traced. On the left side, there was an older pseudarthrosis. The author believes that this confirms Alderson's observation, namely, that the breach in the rib is acquired. He states that there is no reason to suppose a developmental anomaly of ossification, even in a bilateral case.—*Ralph S. Bromer, M.D.*

Keats, Theodore E., Staatz, Dumont S., and Bailey, Robert W. Pneumoarthrography of the knee. *Surg., Gynec. & Obst.*, March, 1952, *94*, 361–364.

Interpretation of the pneumoarthrogram is fundamentally a matter of orientation in the normal anatomy of the knee. The lateral semilunar cartilage is smaller than the medial one and has the configuration of the small letter "o" while the medial meniscus is shaped like the capital letter "C."

The lateral collateral ligament forms a bridge over the lateral aspect of the joint and the popliteus tendon passes beneath this bridge.

The synovial cavity of the knee joint has as many intricacies as the peritoneal cavity. When it is distended with oxygen the semilunar cartilages as well as the articular cartilages and the bone ends stand out sharply. The semilunar cartilages are viewed in cross section and are wedge-shaped with sharply defined margins. The intercondylar area contains a mass of indistinguishable substance, the cruciate ligaments. The bursa of the popliteus tendon appears as a radiolucency at the base of the posterior horn of the lateral meniscus, and occasionally the tendon may be seen in cross section, invaginating this bursa. In views of the body and anterior horn of the lateral meniscus, the popliteus tendon will be seen coursing across the lateral aspect of the joint. The fat pad, and occasionally remnants of the ligamentum mucosum, can be seen on the lateral projection.

A series of 200 pneumoarthrograms performed at the University of Michigan Hospital is covered by this report. Of this number 80 patients were subjected to arthrotomy. A comparison was made of the accuracy of diagnosis of internal derangements of the knee by (1) clinical diagnosis, (2) pneumoarthrogram, (3) combined clinical and pneumoarthrographic evidence. The number of clinical diagnoses, accurate in type of abnormality and its location, was 56, or 70 per cent of the surgically proved cases. A correct pneumoarthrographic diagnosis, without benefit of clinical information, by various members of the Department of Radiology was made 60 times, or in 75 per cent of the cases. A correct diagnosis with the contributions of both clinical and pneumoarthrographic evidence was made 72 times, or in 90 per cent of the cases.

In the 200 instances in which pneumoarthrography was performed, there was not a single complication. —*Mary Frances Vastine, M.D.*

Lauge-Hansen, N. Fractures of the ankle. IV. Clinical use of genetic roentgen diagnosis and genetic reduction. *A.M.A. Arch. Surg.*, April, 1952, *64*, 488–500.

In previous investigative studies the author described four types of fractures of the ankle which were produced experimentally. The pathologic anatomy was determined by dissection and the fractures were genetically classified by experimental roentgenography. The present clinical study was based on 425 ankle fractures, 228 of which were in adults. The roentgenographic appearances of these fractures were classified into four basic types according to their manner of production. The fractures were reduced according to the principles determined by the experimental studies.

The four types of ankle fractures are: (1) the supination-adduction type; (2) the supination-eversion type; (3) the pronation-abduction type; (4) the pronation-eversion type, and are so designated with reference to the position of the foot at the moment of fracture and the forced movement of the foot which produces the fracture. The various types are characterized by the localization and form of the fibular fracture and each type is subdivided accord-

ing to the association of the fibular fracture with additional fractures of other parts of the ankle.

An exact genetic roentgen diagnosis may be made from the roentgenogram and the pathologic anatomy, including various ligamentous ruptures, can be determined.

Roentgenograms demonstrating the various types of fractures and a description of the maneuvers employed in obtaining genetic reduction are included in the paper.—*Gerald Lavner, M.D.*

BRAILSFORD, JAMES F. Chondro-osteo-dystrophy. *J. Bone & Joint Surg.*, Feb., 1952, *34-B*, 53–63.

Chondro-osteo-dystrophy is the name given by Brailsford in 1928 to a disorder of the skeleton which manifests itself during the first three years of life. The child originally described had appeared to be normal at birth but at the age of five months the mother noticed that he developed a kyphosis in the thoracolumbar region. His first roentgen examination was made by the author at the age of three and a half years. These roentgen changes are described together with the clinical course of the patient in detail. From the age of ten he progressively and steadily declined; the musculature became flaccid and atrophied as if in association with the general dystrophic condition of the skeleton. He did not grow, though his limbs appeared long in comparison with his trunk, and his neck appeared to get shorter. Toward the end of his twelfth year of life his facial characteristics became grotesque and when he died at the age of fourteen, after being bedridden for nearly a year, he was but 2 feet 10 inches tall and weighed 28 pounds.

In the paper, Brailsford shows serial roentgenographic evidence of the course of the disease. The period covered is sixteen or more years of life of this patient and of other patients with a similar condition whom he has seen and examined. In the early stages of the disease the roentgen changes in the spine consist of flattening of the vertebral bodies, some of which exhibit an anterior tongue with no ossification in the upper and lower epiphyseal sites, some being slipper-shaped and of irregular size. In the cervicothoracic compression of the bodies there is a shortening of the neck; in the thoracolumbar area, kyphosis has been associated with vertebral bodies, irregular in shape, and disc spaces may be as deep as the flattened vertebral bodies. With increasing flattening of the vertebrae, the sternum is pushed forward progressively. In the extremities, the epiphyses may have multiple ossific areas and the diaphyseal extremities are sometimes irregular in ossification. The joint spaces, more particularly of the shoulder, hip, knee and ankle joint, are considerably widened, suggesting overgrowth of cartilage. The nuclei for the carpal and tarsal bones show delay in development and marked irregularity of outline.

By a study of serial roentgenograms of the skeleton of his cases through life, it was noted that while the skull remained relatively normal the epiphyses of the larger joints, notably the hips, deteriorated. With progressive weakening of the musculature, the joints became unstable and, in some instances, dislocation of the hip occurred. The acetabula expanded to the anterior spine and the upper ends of the femurs came into cartilaginous apposition with the lateral aspect of the ilia. Later this connection was lost and the joints became somewhat flail. At the knee joint, because the epiphyses were ossified from multiple nuclei which have not the stability of the normal entirely homogeneous nuclei, and because the ossification of the diaphyseal extremities was irregular and mechanically unsound, knock-knee deformity developed without any bowing of the shafts of the diaphyses as in rickets.

From the author's study of his cases he regards it as probable that the condition occurs in both sexes and is associated with some lethal factor in the parents producing a state of incompatibility. The gravity of the lethal factor appears to be accentuated by consanguinity of parentage. He feels, however, that the immaturity of parents and the employment of abortifacients cannot be ruled out in one case of a dystrophic child, the offspring of a brother and sister aged sixteen and fourteen years respectively. Syphilis was not detected in any of his cases. In all cases there appeared to be induced an associated constitutional weakness, so great in some as to be incompatible with separate life; in others, less severe, the infant survives a few years then dies from pneumonia, or, as in one case who died at the age of fourteen, from a progressive degeneration of all skeletal tissues. In some, the dystrophy shows progressive development, resulting in dwarfing of the skeleton and weakness of the musculature, but the patient survives to adult life and is of normal or perhaps supernormal intelligence.

The differential diagnosis of the condition from rickets, hypothyroidism, osteochondritis or avascular necrosis, achondroplasia and gargoylism is discussed in detail in the paper. Roentgenograms and clinical photographs of some of the patients are reproduced.—*Ralph S. Bromer, M.D.*